



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/JP90/01340</p> <p>(22) International Filing Date: 18 October 1990 (18.10.90)</p> <p>(30) Priority data:</p> <table border="0"> <tr> <td>1/274338</td> <td>20 October 1989 (20.10.89)</td> <td>JP</td> </tr> <tr> <td>2/66063</td> <td>15 March 1990 (15.03.90)</td> <td>JP</td> </tr> <tr> <td>2/105580</td> <td>20 April 1990 (20.04.90)</td> <td>JP</td> </tr> <tr> <td>2/181858</td> <td>9 July 1990 (09.07.90)</td> <td>JP</td> </tr> </table> <p>(71) Applicant (for all designated States except US): OTSUKA PHARMACEUTICAL COMPANY, LIMITED [JP/JP]; 9, Kandatsukasa-cho 2-chome, Chiyoda-ku, Tokyo 101 (JP).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only): OGAWA, Hidenori [JP/JP]; MIYAMOTO, Hisashi [JP/JP]; 21-3, Yoshinari-Aza-Todoroki, Ojin-cho, Tokushima-shi, Tokushima 771-11 (JP). KONDO, Kazumi [JP/JP]; 19-27, Okuwaji-ma-Aza-Suberitwahama, Muya-cho, Naruto-shi, Tokushima 772 (JP). YAMASHITA, Hiroshi [JP/JP]; 57-1, Sakino-Aza-Hachikami, Matsushige-cho, Itano-gun, Tokushima 771-02 (JP). NAKAYA, Kenji [JP/JP]; 48, Kamibetsukukita, Kawauchi-cho, Tokushima-shi, Tokushima 771-01 (JP). KOMATSU, Hajime [JP/JP]; TANAKA, Michinori [JP/JP]; KORA, Shinya [JP/JP]; 463-10, Kagasuno, Kawauchi-cho, Tokushima-shi, Tokushima 771-01 (JP). TOMINAGA, Michiaki [JP/JP];</p>		1/274338	20 October 1989 (20.10.89)	JP	2/66063	15 March 1990 (15.03.90)	JP	2/105580	20 April 1990 (20.04.90)	JP	2/181858	9 July 1990 (09.07.90)	JP	<p>310-6, Takaiso, Kamiita-cho, Itano-gun, Tokushima 771-13 (JP). YABUUCHI, Yoichi [JP/JP]; 900-25, Omatsu, Kawauchi-cho, Tokushima-shi, Tokushima 771-01 (JP).</p> <p>(74) Agents: AOYAMA, Tamotsu et al.; Twin 21 Mid Tower, 1-61, Shiromi 2-chome, Chuo-ku, Osaka-shi, Osaka 540 (JP).</p> <p>(81) Designated States: AT (European patent), BE (European patent), CH (European patent), DE (European patent), DK (European patent), ES (European patent), FR (European patent), GB (European patent), GR (European patent), IT (European patent), KR, LU (European patent), NL (European patent), SE (European patent), US.</p> <p>Published With international search report.</p>
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<p>(54) Title: BENZOHETEROCYCLIC COMPOUNDS</p> <div style="text-align: center;"> <p>(I)</p> </div> <div style="text-align: center; margin-top: 20px;"> <p>(α)</p> </div> <p>(57) Abstract</p> <p>Novel benzoheterocyclic compounds of formula (I), wherein R<sup>1</sup> is H, halogen, alkyl, optionally substituted amino, alkoxy; R<sup>2</sup> is H, halogen, alkoxy, phenylalkoxy, OH, alkyl, optionally substituted amino, carbamoyl-alkoxy, optionally substituted amino-alkoxy, optionally substituted benzoyloxy; R<sup>3</sup> is a group: -NR<sup>4</sup>R<sup>5</sup> or -CO-NR<sup>11</sup>R<sup>12</sup>; R<sup>4</sup> is H, optionally substituted benzoyl, alkyl; R<sup>5</sup> is a group α [R<sup>16</sup> is halogen, optionally substituted amino, phenyl, cycloalkyl, etc., or a group: -O-A-NR<sup>6</sup>R<sup>7</sup>; m is 0 to 3], phenyl-alkoxycarbonyl, alkanoyl, phenyl-alkanoyl, etc.; R<sup>11</sup> is H or alkyl; R<sup>12</sup> is cycloalkyl or optionally substituted phenyl; and W is a group: -(CH<sub>2</sub>)<sub>p</sub> (p is 3 to 5) or -CH=CH-(CH<sub>2</sub>)<sub>q</sub> (q is 1 to 3), the carbon atom of these groups being optionally replaced by O, S, SO, SO<sub>2</sub> or a group: -N(R<sup>13</sup>)- and further these groups having optionally 1 to 3 substituents of alkyl, alkoxycarbonyl, carboxy, OH, O, alkanoyloxy, etc., which have excellent vasopressin antagonistic activities and are useful as vasodilator, hypotensive agent, water diuretics, platelet agglutination inhibitor, and a vasopressin antagonistic composition containing the compound as the active ingredient.</p>														

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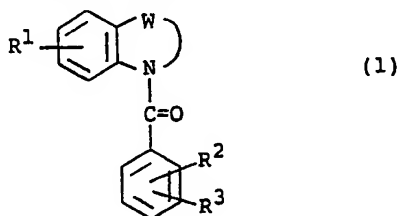
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BENZOHETEROCYCLIC COMPOUNDSTechnical Field

This invention relates to novel benzoheterocyclic compounds which have excellent vasopressin antagonistic activities and are useful as vasodilator, hypotensive agent, water diuretics, platelet aggregation inhibitor.

Disclosure of the Invention

The benzoheterocyclic compounds of this invention have the following formula:



wherein  $R^1$  is hydrogen atom, a halogen atom, a lower alkyl, an amino having optionally a lower alkyl substituent, or a lower alkoxy,

$R^2$  is hydrogen atom, a halogen atom, a lower alkoxy, a phenyl(lower)alkoxy, hydroxy, a lower alkyl, an amino having optionally a lower alkyl substituent, a carbamoyl-substituted lower alkoxy, an amino-substituted lower alkoxy having optionally a lower alkyl substituent, or a benzoyloxy which has optionally a halogen substituent on the phenyl ring,

$R^3$  is a group of the formula:  $-\text{N} \begin{matrix} \text{R}^4 \\ \text{R}^5 \end{matrix}$  or a group of

the formula:  $-\text{C} \begin{matrix} \text{O} \\ \parallel \\ \text{N} \begin{matrix} \text{R}^{11} \\ \text{R}^{12} \end{matrix} \end{matrix}$ ,

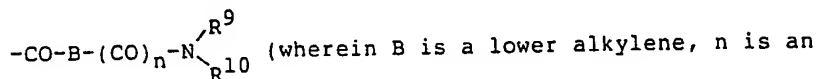
R<sup>4</sup> is hydrogen atom, a benzoyl which has optionally a halogen substituent on the phenyl ring, or a lower alkyl,

R<sup>5</sup> is a group of the formula:  $-\text{CO}-\text{C}_6\text{H}_4-(\text{R}^{16})_m$   
 [wherein R<sup>16</sup> is a halogen atom; a lower alkyl which has optionally a substituent selected from a halogen atom and hydroxy; hydroxy; a lower alkoxy; a lower alkanoyloxy; a lower alkylthio; a lower alkanoyl; carboxy; a lower alkoxycarbonyl; cyano; nitro; an amino which has optionally a substituent selected from a lower alkyl and a lower alkanoyl; phenyl; a cycloalkyl; a lower alkanoyloxy-substituted lower alkoxy; a carboxy-substituted lower alkoxy; a halogen-substituted lower alkoxy; a carbamoyl-substituted lower alkoxy; a hydroxy-substituted lower alkoxy; a lower alkoxycarbonyl-substituted lower alkoxy; a phthalimido-substituted lower alkoxy; an aminocarbonyl-lower alkoxy having a lower alkyl substituent; or a group of the formula:  $-\text{O}-\text{A}-\text{N} \begin{matrix} \text{R}^6 \\ \text{R}^7 \end{matrix}$  (A is a lower alkylene, and R<sup>6</sup> and R<sup>7</sup> are

the same or different and are each hydrogen atom, a lower alkyl having optionally a hydroxy substituent, a lower alkanoyl, or benzoyl, or R<sup>6</sup> and R<sup>7</sup> may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom wherein the heterocyclic group has optionally a substituent selected from piperidinyl and a lower alkyl); and m is an integer of 0 to 3]; a phenyl-lower alkoxycarbonyl, a lower alkanoyl, a phenyl-



lower alkanoyl, a cycloalkyl-lower alkanoyl, a cycloalkyl-carbonyl, tricyclo[3.3.1.1]decanylcarbonyl, naphthyl-carbonyl, pyridylcarbonyl, furoyl, thenoyl, a phenoxy-lower alkanoyl which phenyl ring has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent, a phthalimido-substituted lower alkanoyl, a lower alkoxy-carbonyl-lower alkanoyl, a carboxy-lower alkanoyl, a naphthyloxy-lower alkanoyl, a halogen-substituted lower alkanoyl, a group of the formula:  $\text{-CO-}\langle\text{C}_6\text{H}_4\rangle\text{-N-R}^8$  (wherein  $\text{R}^8$  is hydrogen atom, a lower alkyl, a phenyl-lower alkoxy carbonyl, a carbamoyl-lower alkyl, an amino-lower alkanoyl having optionally a lower alkyl substituent, or a lower alkanoyl), an anilino carbonyl which has optionally a lower alkyl substituent on the phenyl ring, phenoxy carbonyl, a phenylsulfonyl which has optionally a substituent selected from a halogen atom and a lower alkyl on the phenyl ring, quinolylsulfonyl, or a group of the formula:



integer of 0 or 1, and  $\text{R}^9$  and  $\text{R}^{10}$  are the same or different and are each hydrogen atom, a lower alkyl having optionally a hydroxy substituent, a cycloalkyl, a phenyl-lower alkyl, a lower alkanoyl, a lower alkenyl, a phenoxy-lower alkyl, a phenyl which has optionally 1 to 3 substituents selected from an amino-lower alkyl having optionally a lower alkanoyl substituent, a lower alkyl, a lower alkoxy and a halogen atom, a phthalimido-substituted lower alkyl, an amino-lower

alkyl having optionally a lower alkanoyl substituent, a lower alkynyl, or an amino-lower alkyl having optionally a lower alkyl substituent, or  $R^9$  and  $R^{10}$  may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom wherein the heterocyclic group has optionally a substituent selected from a lower alkyl, a lower alkoxy-carbonyl and piperidinyl),

$R^{11}$  is hydrogen atom or a lower alkyl,

$R^{12}$  is a cycloalkyl, or a phenyl which has optionally 1 to 3 substituents selected from a lower alkoxy, a lower alkyl and a halogen atom,

W is a group of the formula:  $-(CH_2)_p-$  (p is an integer of 3 to 5), or a group of the formula:  $-CH=CH-(CH_2)_q-$  (q is an integer of 1 to 3), the carbon atom of these groups:

$-(CH_2)_p-$  and  $-CH=CH-(CH_2)_q-$  being optionally replaced by oxygen atom, sulfur atom, sulfinyl, sulfonyl, or a group of

the formula:  $\begin{matrix} R^{13} \\ | \\ -N- \end{matrix}$  ( $R^{13}$  is hydrogen atom, a cycloalkyl, or a lower alkyl), and further said  $-(CH_2)_p-$  and  $-CH=CH-(CH_2)_q-$  groups having optionally 1 to 3 substituents selected from a lower alkyl having optionally a hydroxy substituent, a lower alkoxy-carbonyl, carboxy, hydroxy, oxo, a lower alkanoyloxy having optionally a halogen substituent, an amino-lower alkyl having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a lower alkanoyloxy-substituted lower alkyl, a lower alkyl sulfonyloxy-lower alkyl, an

azido-lower alkyl, a group of the formula:  $\text{>O}$ , an aminocarbonyloxy having optionally a lower alkyl substituent, a lower alkoxy, a lower alkoxy-carbonyl-substituted lower alkoxy, a carboxy-substituted lower alkoxy, an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent, an amino-lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a phthalimido-substituted lower alkoxy, hydroxyimino, a lower alkanoyloxy-imino, a lower alkylidene, a halogen atom, azido, sulfoxyimino, a group of the formula:  $\text{R}^{81}-\text{N}-\text{CH}_2\text{COO}-$  ( $\text{R}^{81}$  is hydrogen atom or a lower alkyl),

hydrazino, pyrrolyl, an amino-lower alkanoyloxy having optionally a lower alkyl substituent, a group of the formula:  $-\text{O}-\text{A}-\text{CO}-\text{N} \begin{smallmatrix} \text{R}^{82} \\ \text{R}^{83} \end{smallmatrix}$  (A is as defined above, and  $\text{R}^{82}$  and  $\text{R}^{83}$  are the same or different and are each hydrogen atom, a lower alkyl, a carbamoyl-substituted lower alkyl, a hydroxy-substituted lower alkyl, or a pyridyl-lower alkyl, or  $\text{R}^{82}$  and  $\text{R}^{83}$  may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen, oxygen or sulfur atom wherein the heterocyclic group has optionally a substituent selected from oxo, a lower alkyl, a lower alkanoyl, and carbamoyl), and a group of the formula:

$-(\text{CO})_n-\text{N} \begin{smallmatrix} \text{R}^{14} \\ \text{R}^{15} \end{smallmatrix}$  (wherein n is as defined above, and  $\text{R}^{14}$  and  $\text{R}^{15}$

are the same or different and are each hydrogen atom, a lower alkyl, a lower alkenyl, a lower alkanoyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having optionally 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl, benzoyl, a lower alkoxy-carbonyl, anilinocarbonyl, an aminocarbonyl having optionally a lower alkyl substituent, a cyano-substituted lower alkyl, a lower alkoxy-carbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent on the piperidinyl ring, a halogen-substituted lower alkanoyl, an imidazolyl-substituted lower alkanoyl, an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxy-carbonyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a phenyl-lower alkoxy-carbonyl, or  $R^{14}$  and  $R^{15}$  may bind together with nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen, wherein the heterocyclic group may optionally have a substituent selected from a lower alkyl, a phenyl-lower alkyl or a lower alkanoyl).

The benzoheterocyclic compounds of the formula (1) and

their salts have excellent vasopressin antagonistic activities and vasodilating activity, hypotensive activity, activity for inhibiting saccharide release in liver, activity for inhibiting growth of mesangium cells, water diuretic activity, platelet agglutination inhibitory activity and are useful as vasodilator, hypotensive agent, water diuretics, platelet agglutination inhibitor and are used for the prophylaxis and treatment of hypertension, edema, ascites, heart failure, renal function disorder, vasopressin parasecretion syndrome (SIADH), hepatocirrhosis, hyponatremia, hypokaliemia, diabetic, circulation disorder, and the like.

Each group in the above formula (1) includes specifically the following groups.

The "lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, for example, methoxy, ethoxy, propoxy, isopropoxy, butoxy, tert-butoxy, pentyloxy, hexyloxy, and the like.

The "lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl, hexyl, and the like.

The "halogen atom" includes fluorine atom, chlorine atom, bromine atom and iodine atome.

The "amino having optionally a lower alkyl substituent" includes an amino having optionally one or two substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, amino,

methylamino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, dipentylamino, dihexylamino, N-methyl-N-ethylamino, N-ethyl-N-propylamino, N-methyl-N-butylamino, N-methyl-N-hexylamino, and the like.

The "lower alkenyl" includes a straight chain or branched chain alkenyl group having 2 to 6 carbon atoms, for example, vinyl, allyl, 2-butenyl, 3-butenyl, 1-methylallyl, 2-pentenyl, 2-hexenyl, and the like.

The "lower alkyl which has optionally a substituent selected from a halogen atom and hydroxy" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which may optionally have 1 to 3 substituents selected from a halogen atom and hydroxy, for example, in addition to the above-mentioned lower alkyl groups, hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxypropyl, 4-hydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5,5,4-trihydroxypentyl, 5-hydroxypentyl, 6-hydroxyhexyl, 1-hydroxyisopropyl, 2-methyl-3-hydroxypropyl, trifluoromethyl, trichloromethyl, chloromethyl, bromomethyl, fluoromethyl, iodomethyl, difluoromethyl, dibromomethyl, 2-chloroethyl, 2,2,2-trifluoroethyl, 2,2,2-trichloroethyl, 3-chloropropyl, 2,3-dichloropropyl, 4,4,4-trichlorobutyl, 4-fluorobutyl, 5-chloropentyl, 3-chloro-2-methylpropyl, 5-bromohexyl, 5,6-dichlorohexyl, and the like.

The "lower alkylene" includes a straight chain or

branched chain alkylene group having 1 to 6 carbon atoms, for example, methylene, ethylene, trimethylene, 2-methyltrimethylene, 2,2-dimethyltrimethylene, 1-methyltrimethylene, methylmethylene, ethylmethylene, tetramethylene, penta-methylene, hexamethylene, and the like.

The "lower alkanoyloxy" includes a straight chain or branched chain alkanoyloxy group having 1 to 6 carbon atoms, for example, formyloxy, acetyloxy, propionyloxy, butyryloxy, isobutyryloxy, pentanoyloxy, tert-butylcarbonyloxy, hexanoyloxy, and the like.

The "lower alkylthio" includes a straight chain or branched chain alkylthio group having 1 to 6 carbon atoms, for example, methylthio, ethylthio, propylthio, isopropylthio, butylthio, tert-butylthio, pentylthio, hexylthio, and the like.

The "lower alkanoyl" includes a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, formyl, acetyl, propionyl, butyryl, isobutyryl, pentanoyl, tert-butylcarbonyl, hexanoyl, and the like.

The "lower alkoxycarbonyl" includes a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms in the alkoxy moiety, for example, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, isopropoxycarbonyl, butoxycarbonyl, tert-butoxycarbonyl, pentyloxycarbonyl, hexyloxy-carbonyl, and the like.

The "amino having optionally a substituent selected from a lower alkyl and a lower alkanoyl" includes an amino having optionally one or two substituents selected from a

straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, amino, methyl-amino, ethylamino, propylamino, isopropylamino, butylamino, tert-butylamino, pentylamino, hexylamino, dimethylamino, diethylamino, dipropylamino, dibutylamino, dipentylamino, dihexylamino, N-methyl-N-ethylamino, N-ethyl-N-propylamino, N-methyl-N-butylamino, N-methyl-N-hexylamino, N-methyl-N-acetyl-amino, N-acetylamino, N-formylamino, N-propionylamino, N-butyrylamino, N-isobutyrylamino, N-pentanoylamino, N-tert-butylcarbonylamino, N-hexanoylamino, N-ethyl-N-acetylamino, and the like.

The "cycloalkyl" includes a cycloalkyl having 3 to 8 carbon atoms, for example, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl, and the like.

The "lower alkanoyloxy-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by a straight chain or branched chain alkanoyloxy group having 2 to 6 carbon atoms, for example, acetyloxymethoxy, 2-propionyloxyethoxy, 1-butyryloxyethoxy, 3-acetyloxypropoxy, 4-acetyloxybutoxy, 4-isobutyryloxybutoxy, 5-pentanoyloxypropyloxy, 6-acetyloxyhexyloxy, 6-tert-butylcarbonyloxyhexyloxy, 1,1-dimethyl-2-hexanoyloxyethoxy, 2-methyl-3-acetyloxypropoxy, and the like.

The "carbamoyl-substituted lower alkoxy" includes a carbamoyl-substituted alkoxy group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 6



carbon atoms, for example, carbamoylmethoxy, 2-carbamoylethoxy, 1-carbamoylethoxy, 3-carbamoylpropoxy, 4-carbamoylbutoxy, 5-carbamoylpentyloxy, 6-carbamoylhexyloxy, 1,1-dimethyl-2-carbamoylethoxy, 2-methyl-3-carbamoylpropoxy, and the like.

The "hydroxy-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms and having 1 to 3 hydroxy substituents, for example, hydroxymethoxy, 2-hydroxyethoxy, 1-hydroxyethoxy, 3-hydroxypropoxy, 2,3-dihydroxypropoxy, 4-hydroxybutoxy, 3,4-dihydroxybutoxy, 1,1-dimethyl-2-hydroxyethoxy, 5-hydroxypentyloxy, 6-hydroxyhexyloxy, 2-methyl-3-hydroxypropoxy, 2,3,4-trihydroxybutoxy, and the like.

The "lower alkoxycarbonyl-substituted lower alkoxy" includes an alkoxycarbonyl-substituted straight chain or branched chain alkoxy group having 1 to 6 carbon atoms wherein the alkoxycarbonyl moiety is a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, methoxycarbonylmethoxy, 3-methoxycarbonylpropoxy, ethoxycarbonylmethoxy, 3-ethoxycarbonylpropoxy, 4-ethoxycarbonylbutoxy, 5-isopropoxycarbonylpentyloxy, 6-propoxycarbonylhexyloxy, 1,1-dimethyl-2-butoxycarbonylethoxy, 2-methyl-3-tert-butoxycarbonylpropoxy, 2-pentyloxycarbonylethoxy, hexyloxycarbonylmethoxy, and the like.

The "carboxy-substituted lower alkoxy" includes a carboxy-substituted alkoxy group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, for example, carboxymethoxy, 2-carboxyethoxy, 1-

carboxyethoxy, 3-carboxypropoxy, 4-carboxybutoxy, 5-carboxypentyloxy, 6-carboxyhexyloxy, 1,1-dimethyl-2-carboxyethoxy, 2-methyl-3-carboxypropoxy, and the like.

The "phthalimido-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by phthalimido group, for example, phthalimidomethoxy, 2-phthalimidoethoxy, 1-phthalimidoethoxy, 3-phthalimidopropoxy, 4-phthalimidobutoxy, 5-phthalimidopentyloxy, 6-phthalimidohexyloxy, 1,1-dimethyl-2-phthalimidoethoxy, 2-methyl-3-phthalimidopropoxy, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups  $R^6$  and  $R^7$  together with the nitrogen atom to which they bond with or without being intervened with nitrogen or oxygen atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, and the like.

The "heterocyclic group having a substituent selected from piperidinyl and a lower alkyl" includes a heterocyclic group having 1 to 3 substituents selected from piperidinyl and a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, 4-methylpiperiazinyl, 3,4-dimethylpiperazinyl, 3-ethylpyrrolidinyl, 2-propylpyrrolidinyl, 3,4,5-trimethylpiperidinyl, 4-butylpiperidinyl, 3-pentylmorpholino, 4-hexylpiperazinyl, 4-(1-piperidinyl)piperidinyl, 3-(1-piperidinyl)pyrrolidinyl, 3-(1-piperidinyl)-4-methylpiperazinyl, 3-(1-piperidinyl)morpholino, and the like.

The "phenyl(lower)alkanoyl" includes a phenylalkanoyl wherein the alkanoyl moiety is a straight chain or branched

chain alkanoyl group having 2 to 6 carbon atoms, for example, phenylacetyl, 3-phenylpropionyl, 2-phenylpropionyl, 4-phenylbutyryl, 2,2-dimethyl-3-phenylpropionyl, 5-phenylpentanoyl, 6-phenylhexanoyl, and the like.

The "cycloalkyl-lower alkanoyl" includes  $C_3-C_8$  cycloalkyl-alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, cyclohexylacetyl, 3-cyclopropylpropionyl, 2-cyclopentylpropionyl, 4-cyclohexylbutyryl, 2,2-dimethyl-3-cycloheptylpropionyl, 5-cyclooctylpentanoyl, 6-cyclohexylhexanoyl, and the like.

The "cycloalkylcarbonyl" includes a cycloalkylcarbonyl having 3 to 8 carbon atoms, for example, cyclopropylcarbonyl, cyclobutylcarbonyl, cyclopentylcarbonyl, cyclohexylcarbonyl, cycloheptylcarbonyl, cyclooctylcarbonyl, and the like.

The "amino having optionally a lower alkanoyl substituent" includes an amino having optionally a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, amino, formylamino, acetylamino, propionylamino, butyrylamino, isobutyrylamino, pentanoylamino, tert-butylcarbonylamino, hexanoylamino, and the like.

The "phenoxy-lower alkanoyl which phenyl ring has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent" includes a phenoxyalkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms and the phenyl ring has optionally 1

to 3 substituents selected from a straight chain or branched chain alkyl having 1 to 6 carbon atoms, a straight chain or branched chain alkoxy having 1 to 6 carbon atoms and an amino having optionally a straight chain or branched chain alkanoyl having 1 to 6 carbon atoms, for example, phenoxyacetyl, 3-phenoxypropionyl, 2-phenoxypropionyl, 4-phenoxybutyryl, 2,2-dimethyl-3-phenoxypropionyl, 5-phenoxy-pentanoyl, 6-phenoxy-hexanoyl, (2-aminophenoxy)acetyl, 3-(4-aminophenoxy)propionyl, (2-methylphenoxy)acetyl, (4-methylphenoxy)acetyl, (3-methylphenoxy)acetyl, (3-methoxyphenoxy)acetyl, (3-acetylaminophenoxy)acetyl, 4-(2-propionylaminophenoxy)butyryl, 2,2-dimethyl-3-(4-butyrylaminophenoxy)propionyl, 5-(2-pentanoylaminophenoxy)pentanoyl, 6-(4-hexanoylaminophenoxy)hexanoyl, 3-(2-ethylphenoxy)propionyl, 2-(4-propylphenoxy)propionyl, 4-(4-butylphenoxy)butyryl, 5-(3-pentylphenoxy)pentanoyl, 6-(4-hexylphenoxy)hexanoyl, (2,3-dimethylphenoxy)acetyl, (2,5-dimethylphenoxy)acetyl, (3,4-dimethylphenoxy)acetyl, (3,4,5-trimethylphenoxy)acetyl, 3-(4-methoxyphenoxy)propionyl, 2-(2-propoxyphenoxy)propionyl, 4-(3-butoxyphenoxy)butyryl, 5-(4-pentyloxyphenoxy)pentanoyl, 6-(4-hexyloxyphenoxy)hexanoyl, (3,4-dimethoxyphenoxy)acetyl, (3,5-dimethoxyphenoxy)acetyl, (2,4-dimethoxyphenoxy)acetyl, (3,4,5-trimethoxyphenoxy)acetyl, (2-acetyl-amino-4-methylphenoxy)acetyl, (4-acetyl-amino-3-methoxyphenoxy)acetyl, and the like.

The "phthalimido-substituted lower alkanoyl" includes a straight chain or branched chain alkanoyl group having 2 to 6 carbon atoms which is substituted by phthalimido group, for

example, 2-phthalimidoacetyl, 3-phthalimidopropionyl, 2-phthalimidopropionyl, 4-phthalimidobutyryl, 2,2-dimethyl-3-phthalimidopropionyl, 5-phthalimidopentanoyl, 6-phthalimidohexanoyl, 3-methyl-4-phthalimidobutyryl, and the like.

The "lower alkoxycarbonyl-lower alkanoyl" includes an alkoxycarbonyl-alkanoyl group wherein the alkoxy moiety is a straight chain or branched chain alkoxy having 1 to 6 carbon atoms and the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, methoxycarbonylacetyl, 3-methoxycarbonylpropionyl, ethoxycarbonylacetyl, 3-ethoxycarbonylpropionyl, 4-ethoxycarbonylbutyryl, 3-propoxycarbonylpropionyl, 2-methoxycarbonylpropionyl, 6-propoxycarbonylhexanoyl, 5-isopropoxycarbonylpentanoyl, 2,2-dimethyl-3-butoxycarbonylpropionyl, 2-methyl-3-tert-butoxycarbonylpropionyl, pentyloxycarbonylacetyl, hexyloxycarbonylacetyl, and the like.

The "carboxy-lower alkanoyl" includes a carboxy-alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, carboxyacetyl, 3-carboxypropionyl, 2-carboxypropionyl, 4-carboxybutyryl, 2,2-dimethyl-3-carboxypropionyl, 5-carboxypentanoyl, 6-carboxyhexanoyl, and the like.

The "naphthyloxy-lower alkanoyl" includes a naphthyl-oxy-alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms, for example, naphtyloxyacetyl, 3-naphtyloxypropionyl, 2-naphtyloxypropionyl, 4-naphthyloxybutyryl, 2,2-dimethyl-3-

naphthyloxypropionyl, 5-naphthyloxypentanoyl, 6-naphthyloxyhexanoyl, and the like.

The "phenyl-lower alkoxycarbonyl" includes a phenyl-alkoxycarbonyl wherein the alkoxycarbonyl moiety is a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, benzyloxycarbonyl, 2-phenylethoxycarbonyl, 1-phenylethoxycarbonyl, 3-phenylpropoxycarbonyl, 4-phenylbutoxycarbonyl, 5-phenylpentoxycarbonyl, 6-phenylhexyloxycarbonyl, 1,1-dimethyl-2-phenylethoxycarbonyl, 2-methyl-3-phenylpropoxycarbonyl, and the like.

The "lower alkyl having optionally a hydroxy substituent" includes a straight chain or branched chain alkyl having 1 to 6 carbon atoms and having optionally 1 to 3 hydroxy substituents, for example, hydroxymethyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxyethyl, 4-hydroxybutyl, 3,4-dihydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5-hydroxypentyl, 6-hydroxyhexyl, 2-methyl-3-hydroxypropyl, 2,3,4-trihydroxybutyl, and the like.

The "phenyl-lower alkyl" includes a phenylalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, benzyl, 2-phenylethyl, 1-phenylethyl, 3-phenylpropyl, 4-phenylbutyl, 5-phenylpentyl, 6-phenylhexyl, 1,1-dimethyl-2-phenylethyl, 2-methyl-3-phenylpropyl, and the like.

The "phenoxy-lower alkyl" includes a phenoxyalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example,

phenoxymethyl, 1-phenoxyethyl, 2-phenoxyethyl, 3-phenoxypropyl, 4-phenoxybutyl, 5-phenoxypentyl, 6-phenoxyhexyl, 1,1-dimethyl-2-phenoxyethyl, 2-methyl-3-phenoxypropyl, and the like.

The "phenyl which has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and a halogen atom" includes a phenyl group which has optionally 1 to 3 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms and a halogen atom, for example, phenyl, 2-methoxyphenyl, 3-methoxyphenyl, 4-methoxyphenyl, 2-ethoxyphenyl, 3-ethoxyphenyl, 4-ethoxyphenyl, 4-isopropoxyphenyl, 4-pentyloxyphenyl, 2,4-dimethoxyphenyl, 4-hexyloxyphenyl, 3,4-dimethoxyphenyl, 3-ethoxy-4-methoxyphenyl, 2,3-dimethoxyphenyl, 3,4-diethoxyphenyl, 2,5-dimethoxyphenyl, 2,6-dimethoxyphenyl, 3,5-dimethoxyphenyl, 3,4-dipentyloxyphenyl, 3,4,5-trimethoxyphenyl, 2-chlorophenyl, 3-chlorophenyl, 4-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, 4-fluorophenyl, 2-bromophenyl, 3-bromophenyl, 4-bromophenyl, 2-iodophenyl, 3-iodophenyl, 4-iodophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 2,6-dichlorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 3,4-difluorophenyl, 3,5-dibromophenyl, 3,4,5-trichlorophenyl, 2-methoxy-3-chlorophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylphenyl, 2-ethylphenyl, 3-ethylphenyl, 4-ethylphenyl, 4-isopropylphenyl, 3-butylphenyl, 4-pentylphenyl, 4-hexylphenyl, 3,4-dimethylphenyl, 3,4-diethylphenyl, 2,4-dimethylphenyl, 2,5-dimethylphenyl, 2,6-dimethylphenyl, 3,4,5-trimethylphenyl, 3-chloro-4-methylphenyl, 3-methoxy-4-methyl-5-

iodophenyl, 3,4-dimethoxy-5-bromophenyl, 3,5-diiodo-4-methoxyphenyl, and the like.

The "amino-lower alkyl having optionally a lower alkyl substituent" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, methylamino-methyl, 1-ethylaminoethyl, 2-propylaminoethyl, 3-isopropyl-aminopropyl, 4-butylaminobutyl, 5-pentylaminopentyl, 6-hexyl-aminohexyl, dimethylaminomethyl, (N-ethyl-N-propylamino)methyl, 2-(N-methyl-N-hexylamino)ethyl, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups  $R^9$  and  $R^{10}$  together with the nitrogen atom to which they bond with or without being intervened with nitrogen or oxygen atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, and the like.

The "heterocyclic group having a substituent selected from a lower alkyl, a lower alkoxy carbonyl and piperidinyl" includes a heterocyclic group having 1 to 3 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, a straight chain or branched chain alkoxy carbonyl having 1 to 6 carbon atoms and piperidinyl, for example, in addition to the above-mentioned heterocyclic groups



having a substituent of a lower alkyl and piperidinyl, 4-methoxycarbonylpiperazinyl, 4-ethoxycarbonylpiperidinyl, 3-propoxycarbonylpyrrolidinyl, 2-pentyloxycarbonylmorpholino, 4-hexyloxycarbonylpiperidinyl, 4-ethoxycarbonyl-3-methylpiperidinyl, 3-methyl-4-ethoxycarbonylpiperazinyl, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups  $R^{14}$  and  $R^{15}$  together with the nitrogen atom to which they bond with or without being intervened with nitrogen or oxygen atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, and the like.

The "heterocyclic group having a lower alkyl substituent" includes a heterocyclic group having 1 to 3 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, 4-methylpiperazinyl, 3,4-dimethylpiperazinyl, 3-ethylpyrrolidinyl, 2-propylpyrrolidinyl, 3,4,5-trimethylpiperidinyl, 4-butylpiperidinyl, 3-pentylmorpholino, 4-hexylpiperazinyl, and the like.

The heterocyclic ring in the formula (1) includes tetrahydroquinolyl, 2,3,4,5-tetrahydro-1H-benzazepinyl, 1,2,3,4,5,6-hexahydrobenzazocinyl, 1,2-dihydroquinolyl, 2,3-dihydro-1H-benzazepinyl, 1,2,3,4-tetrahydrobenzazocinyl, and the like.

The heterocyclic ring in the formula (1) wherein the carbon atom in the group of the formula:  $-(CH_2)_p^-$  or  $-CH=CH-(CH_2)_q^-$  for W is replaced by oxygen atom, sulfur atom,

sulfinyl, sulfonyl, or a group of the formula:  $\begin{array}{c} \text{R}^{13} \\ | \\ -\text{N}- \end{array}$  ( $\text{R}^{13}$  is hydrogen atom or a lower alkyl) includes a heterocyclic group wherein the carbon atom in the group of the formula:  $-(\text{CH}_2)_p^-$  or  $-\text{CH}=\text{CH}-(\text{CH}_2)_q^-$  for W is replaced by oxygen atom, sulfur atom, sulfinyl, sulfonyl, or a group of the formula:  $\begin{array}{c} \text{R}^{13} \\ | \\ -\text{N}- \end{array}$  ( $\text{R}^{13}$  is hydrogen atom or a straight chain or branched chain alkyl having 1 to 6 carbon atoms), for example, 3,4-dihydro-2H-1,4-benzoxazinyl, 1,2,3,5-tetrahydro-4,1-benzoxazepinyl, 1,2,3,4-tetrahydroquinoxaliny, 1,2,3,4,5,6-hexahydro-1,5-benzodiazocinyl, 5-methyl-1,2,3,4,5,6-hexahydro-1,5-benzodiazocinyl, 4-methyl-1,2,3,4-tetrahydroquinoxaliny, 1,2,3,4-tetrahydro-5,1-benzoxazepinyl, 3,4-dihydro-2H-1,4-benzothiazinyl, 2,3,4,5-tetrahydro-1,5-benzothiazepinyl, 1,2,3,5-tetrahydro-4,1-benzothiazepinyl, 4-ethyl-1,2,3,4-tetrahydroquinoxaliny, 4-propyl-1,2,3,4-tetrahydroquinoxaliny, 4-butyl-1,2,3,4-tetrahydroquinoxaliny, 4-pentyl-1,2,3,4-tetrahydroquinoxaliny, 4-hexyl-1,2,3,4-tetrahydroquinoxaliny, 2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-ethyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-propyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-butyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-pentyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 4-hexyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepinyl, 2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-ethyl-2,3,4,5-tetrahydro-1H-1,5-benzo-

diazepinyl, 5-propyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-butyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-pentyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 5-hexyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepinyl, 3,4-dihydro-1-oxo-2H-1,4-benzothiazepinyl, 3,4-dihydro-1,1-dioxo-2H-1,4-benzothiazepinyl, 1-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepinyl, 1,1-dioxo-2,3,4,5-tetrahydro-1,5-benzothiazepinyl, 4-oxo-1,2,3,5-tetrahydro-4,1-benzothiazepinyl, 4,4-dioxo-1,2,3,5-tetrahydro-4,1-benzothiazepinyl, and the like.

The "halogen-substituted lower alkoxy" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which has 1 to 3 substituents of a halogen atom, for example, trifluoromethoxy, trichloromethoxy, chloromethoxy, bromomethoxy, fluoromethoxy, iodomethoxy, difluoromethoxy, dibromomethoxy, 2-chloroethoxy, 2,2,2-trifluoroethoxy, 2,2,2-trichloroethoxy, 3-chloropropoxy, 2,3-dichloropropoxy, 4,4,4-trichlorobutoxy, 4-fluorobutoxy, 5-chloropentyloxy, 3-chloro-2-methylpropoxy, 6-bromohexyloxy, 5,6-dichlorohexyloxy, and the like.

The "halogen-substituted lower alkanoyl" includes a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms which has 1 to 3 substituents of a halogen atom, for example, 2,2,2-trifluoroacetyl, 2,2,2-trichloroacetyl, 2-chloroacetyl, 2-bromoacetyl, 2-fluoroacetyl, 2-iodoacetyl, 2,2-difluoroacetyl, 2,2-dibromoacetyl, 3,3,3-trifluoropropionyl, 3,3,3-trichloropropionyl, 3-chloropropionyl, 2,3-dichloropropionyl, 4,4,4-trichlorobutyryl, 4-fluorobutyryl, 5-

chloropentanoyl, 3-chloro-2-methylpropionyl, 6-bromohexanoyl, 5,6-dibromohexanoyl, and the like.

The "aminocarbonyl-lower alkoxy having a lower alkyl substituent" includes a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by an aminocarbonyl group having 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methylaminocarbonylmethoxy, 1-ethylaminocarbonylethoxy, 2-propylaminocarbonylethoxy, 3-isopropylaminocarbonylpropoxy, 4-butylaminocarbonylbutoxy, 5-pentylaminocarbonylpentyloxy, 6-hexylaminocarbonylhexyloxy, dimethylaminocarbonylmethoxy, 3-diethylaminocarbonylpropoxy, diethylaminocarbonylmethoxy, (N-ethyl-N-propylamino)carbonylmethoxy, 2-(N-methyl-N-hexylamino)carbonylethoxy, and the like.

The "carbamoyl-lower alkyl" includes a carbamoyl-substituted alkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, carbamoylmethyl, 2-carbamoylethyl, 1-carbamoylethyl, 3-carbamoylpropyl, 4-carbamoylbutyl, 5-carbamoylpentyl, 6-carbamoylhexyl, 1,1-dimethyl-2-carbamoylethyl, 2-methyl-3-carbamoylpropyl, and the like.

The "amino-lower alkanoyl having optionally a lower alkyl substituent" includes a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, 2-aminoacetyl, 3-aminopropionyl, 2-aminopropionyl,

4-aminobutyryl, 5-aminopentanoyl, 6-aminohexanoyl, 2,2-dimethyl-3-aminopropionyl, 2-methyl-3-aminopropionyl, 2-methyl-aminoacetyl, 2-ethylaminopropionyl, 3-propylaminopropionyl, 3-isopropylaminopropionyl, 4-butyraminobutyryl, 5-pentylamino-pentanoyl, 6-hexylaminohexanoyl, 2-dimethylaminoacetyl, 2-diethylaminoacetyl, 2-(N-ethyl-N-propylamino)acetyl, 3-(N-methyl-N-hexylamino)propionyl, and the like.

The "amino-lower alkyl having optionally a lower alkanoyl substituent" includes a straight chain or branched chain alkyl having 1 to 6 carbon atoms which is substituted by an amino group having optionally a substituent of a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, acetyl-amino-methyl, 1-acetylaminomethyl, 2-propionylaminomethyl, 3-isopropionylaminopropyl, 4-butyrylaminoethyl, 5-pentanoylamino-pentyl, 6-hexanoylaminoethyl, formylaminomethyl, and the like.

The "anilinocarbonyl having optionally a lower alkyl substituent on the phenyl ring" includes an anilinocarbonyl group having optionally 1 to 3 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms on the phenyl ring, for example, anilinocarbonyl, 2-methylanilino-carbonyl, 3-methylanilinocarbonyl, 4-methylanilinocarbonyl, 2-ethylanilinocarbonyl, 3-ethylanilinocarbonyl, 4-ethylanilino-carbonyl, 4-isopropylanilinocarbonyl, 3-butylianilinocarbonyl, 4-pentylanilinocarbonyl, 4-hexylanilinocarbonyl, 3,4-dimethyl-

anilinocarbonyl, 3,4-diethylanilinocarbonyl, 2,4-dimethylanilinocarbonyl, 2,5-dimethylanilinocarbonyl, 2,6-dimethylanilinocarbonyl, 3,4,5-trimethylanilinocarbonyl, and the like.

The "phenylsulfonyl which has optionally a substituent selected from a halogen and a lower alkyl on the phenyl ring" includes a phenylsulfonyl group which has optionally 1 to 3 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a halogen atom, for example, phenylsulfonyl, 2-chlorophenylsulfonyl, 3-chlorophenylsulfonyl, 4-chlorophenylsulfonyl, 2-fluorophenylsulfonyl, 3-fluorophenylsulfonyl, 4-fluorophenylsulfonyl, 2-bromophenylsulfonyl, 3-bromophenylsulfonyl, 4-bromophenylsulfonyl, 2-iodophenylsulfonyl, 3-iodophenylsulfonyl, 4-iodophenylsulfonyl, 3,4-dichlorophenylsulfonyl, 3,5-dichlorophenylsulfonyl, 2,6-dichlorophenylsulfonyl, 2,3-dichlorophenylsulfonyl, 2,4-dichlorophenylsulfonyl, 3,4-difluorophenylsulfonyl, 3,5-dibromophenylsulfonyl, 3,4,5-trichlorophenylsulfonyl, 2-ethyl-3-chlorophenylsulfonyl, 2-methylphenylsulfonyl, 3-methylphenylsulfonyl, 4-methylphenylsulfonyl, 2-ethylphenylsulfonyl, 3-ethylphenylsulfonyl, 4-ethylphenylsulfonyl, 4-isopropylphenylsulfonyl, 3-butylphenylsulfonyl, 4-pentylphenylsulfonyl, 4-hexylphenylsulfonyl, 3,4-dimethylphenylsulfonyl, 3,4-diethylphenylsulfonyl, 2,4-dimethylphenylsulfonyl, 2,5-dimethylphenylsulfonyl, 2,6-dimethylphenylsulfonyl, 3,4,6-trimethylphenylsulfonyl, 3,4,5-trimethylphenylsulfonyl, 3-chloro-4-methylphenylsulfonyl, 4-methyl-5-iodophenylsulfonyl, 3,4-dimethyl-5-bromophenylsulfonyl, 3,5-diiodo-4-methylphenylsulfonyl,

and the like.

The "phthalimido-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by phthalimido group, for example, phthalimidomethyl, 2-phthalimidoethyl, 1-phthalimidoethyl, 3-phthalimidopropyl, 4-phthalimidobutyl, 5-phthalimidopentyl, 6-phthalimidoethyl, 1,1-dimethyl-2-phthalimidoethyl, 2-methyl-3-phthalimidopropyl, and the like.

The "lower alkynyl" includes a straight chain or branched chain alkynyl having 2 to 6 carbon atoms, for example, ethynyl, 2-propynyl, 2-butyne, 3-butyne, 1-methyl-2-propynyl, 2-pentyne, 2-hexynyl, and the like.

The "benzoyl which has optionally a halogen substituent on the phenyl ring" includes a benzoyl group which has optionally 1 to 3 substituents of a halogen atom on the phenyl ring, for example, benzoyl, 2-chlorobenzoyl, 3-chlorobenzoyl, 4-chlorobenzoyl, 2-fluorobenzoyl, 3-fluorobenzoyl, 4-fluorobenzoyl, 2-bromobenzoyl, 3-bromobenzoyl, 4-bromobenzoyl, 2-iodobenzoyl, 3-iodobenzoyl, 4-iodobenzoyl, 3,4-dichlorobenzoyl, 3,5-dichlorobenzoyl, 2,6-dichlorobenzoyl, 2,3-dichlorobenzoyl, 2,4-dichlorobenzoyl, 3,4-difluorobenzoyl, 3,5-dibromobenzoyl, 3,4,5-trichlorobenzoyl, and the like.

The "phenyl-lower alkoxy" includes a phenylalkoxy group wherein the alkoxy moiety is a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, for

example, benzyloxy, 2-phenylethoxy, 1-phenylethoxy, 3-phenylpropoxy, 4-phenylbutoxy, 5-phenylpentyloxy, 6-phenylhexyloxy, 1,1-dimethyl-2-phenylethoxy, 2-methyl-3-phenylpropoxy, and the like.

The "amino-lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl" include a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, aminomethoxy, 2-aminoethoxy, 1-aminoethoxy, 3-aminopropoxy, 4-aminobutoxy, 5-aminopentyloxy, 6-aminohexyloxy, 1,1-dimethyl-2-aminoethoxy, 2-methyl-3-aminopropoxy, acetylaminomethoxy, 1-acetylaminomethoxy, 2-propionylaminomethoxy, 3-isopropionylaminopropoxy, 4-butyrylaminobutoxy, 5-pentanoylaminopentyloxy, 6-hexanoylaminohexyloxy, formylaminomethoxy, methylaminomethoxy, 1-ethylaminomethoxy, 2-propylaminomethoxy, 3-isopropylaminopropoxy, 4-butylaminobutoxy, 5-pentylaminopentyloxy, 6-hexylaminohexyloxy, dimethylaminomethoxy, (N-ethyl-N-propylamino)methoxy, 2-(N-methyl-N-hexylamino)ethoxy, and the like.

The "benzyloxy which has optionally a halogen substituent on the phenyl ring" includes a benzyloxy group which has optionally 1 to 3 substituents of a halogen atom on the phenyl ring, for example, benzyloxy, 2-chloro-



benzoyloxy, 3-chlorobenzoyloxy, 4-chlorobenzoyloxy, 2-fluorobenzoyloxy, 3-fluorobenzoyloxy, 4-fluorobenzoyloxy, 2-bromobenzoyloxy, 3-bromobenzoyloxy, 4-bromobenzoyloxy, 2-iodobenzoyloxy, 3-iodobenzoyloxy, 4-iodobenzoyloxy, 3,4-dichlorobenzoyloxy, 3,5-dichlorobenzoyloxy, 2,6-dichlorobenzoyloxy, 2,3-dichlorobenzoyloxy, 2,4-dichlorobenzoyloxy, 3,4-difluorobenzoyloxy, 3,5-dibromobenzoyloxy, 3,4,5-trichlorobenzoyloxy, and the like.

The "lower alkanoyloxy-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by a straight chain or branched chain alkanoyloxy group having 2 to 6 carbon atoms, for example, acetyloxymethyl, 2-propionyloxyethyl, 1-butyryloxyethyl, 3-acetyloxypropyl, 4-acetyloxybutyl, 4-isobutyryloxybutyl, 5-pentanoyloxypropyl, 6-acetyloxyhexyl, 6-tert-butylcarbonyloxyhexyl, 1,1-dimethyl-2-hexanoyloxyethyl, 2-methyl-3-acetyloxypropyl, and the like.

The "lower alkylsulfonyloxy-lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by a straight chain or branched chain alkylsulfonyloxy group having 1 to 6 carbon atoms, for example, methylsulfonyloxymethyl, 1-ethylsulfonyloxyethyl, 2-propylsulfonyloxyethyl, 3-isopropylsulfonyloxypropyl, 4-butylsulfonyloxybutyl, 5-pentylsulfonyloxypropyl, 6-hexylsulfonyloxyhexyl, 1,1-dimethyl-2-methylsulfonyloxyethyl, 2-methyl-3-ethylsulfonyloxypropyl, and the

like.

The "azido-lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an azido group, for example, azidomethyl, 1-azidoethyl, 2-azidoethyl, 3-azidopropyl, 4-azidobutyl, 5-azidopentyl, 6-azidohexyl, 1,1-dimethyl-2-azidoethyl, 2-methyl-3-azidopropyl, and the like.

The "lower alkanoyloxyimino" includes a straight chain or branched chain alkanoyloxyimino group having 1 to 6 carbon atoms, for example, formyloxyimino, acetyloxyimino, propionyloxyimino, butyryloxyimino, isobutyryloxyimino, pentanoyloxyimino, tert-butylcarbonyloxyimino, hexanoyloxyimino, and the like.

The "lower alkylidene" includes a straight chain or branched chain alkylidene group having 1 to 6 carbon atoms, for example, methylenidene, ethylenidene, propylenidene, isopropylidene, butylidene, pentylenidene, hexylenidene, and the like.

The "oxiranyl-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by oxiranyl group, for example, oxiranylmethyl, 1-oxiranylethyl, 2-oxiranylethyl, 3-oxiranylpropyl, 4-oxiranylbutyl, 5-oxiranylpentyl, 6-oxiranylhhexyl, 1,1-dimethyl-2-oxiranylethyl, 2-methyl-3-oxiranylpropyl, and the like.

The "lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having

optionally a lower alkyl substituent" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and having 1 to 2 substituents selected from a straight chain or branched chain alkoxy group having 1 to 6 carbon atoms, hydroxy and an amino having optionally a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methoxymethyl, 1-ethoxyethyl, 2-propoxyethyl, 3-isopropoxypropyl, 4-butoxybutyl, 5-pentyl-oxypropyl, 6-hexyloxyhexyl, 1,1-dimethyl-2-methoxyethyl, 2-methyl-3-ethoxypropyl, 3-methoxy-2-hydroxypropyl, hydroxy-methyl, 2-hydroxyethyl, 1-hydroxyethyl, 3-hydroxypropyl, 2,3-dihydroxyethyl, 4-hydroxybutyl, 3,4-dihydroxybutyl, 1,1-dimethyl-2-hydroxyethyl, 5,6-dihydroxyhexyl, 5-hydroxy-pentyl, 6-hydroxyhexyl, 6-(N-ethyl-N-methylamino)-5-methoxy-hexyl, 2-methyl-3-hydroxypropyl, aminomethyl, 1-aminoethyl, 2-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-amino-propyl, methylaminomethyl, ethylaminomethyl, propylamino-methyl, isopropylaminomethyl, butylaminomethyl, tert-butylaminomethyl, pentylaminomethyl, hexylaminomethyl, dimethylaminomethyl, diethylaminomethyl, dipropylamino-methyl, dibutylaminomethyl, dipentylaminomethyl, dihexyl-aminomethyl, N-methyl-N-ethylaminomethyl, N-methyl-N-propylaminomethyl, N-methyl-N-butylaminomethyl, N-methyl-N-hexylaminomethyl, 1-methylaminoethyl, 2-ethylaminoethyl, 3-propylaminopropyl, 4-butylaminobutyl, 1,1-dimethyl-2-pentyl-aminoethyl, 5-hexylaminopentyl, 6-dimethylaminohexyl, 4-

dimethylaminobutyl, 2-diethylaminoethyl, 1-(N-methyl-N-hexylamino)ethyl, 3-diethylaminopropyl, 6-diethylaminoethyl, 4-dibutylaminobutyl, 2-(N-methyl-N-pentylamino)ethyl, 2-hydroxy-3-diethylaminopropyl, 3-hydroxy-4-methylaminobutyl, 5-hydroxy-6-diethylaminoethyl, 4-hydroxy-5-dimethylaminopentyl, 4-hydroxy-5-methylaminopentyl, 4-hydroxy-5-diethylaminopentyl, 5-hydroxy-6-ethylaminoethyl, 5-hydroxy-6-isopropylaminoethyl, 5-hydroxy-6-aminoethyl, and the like.

The "aminocarbonyloxy having optionally a lower alkyl substituent" includes an aminocarbonyloxy group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, aminocarbonyloxy, methylaminocarbonyloxy, ethylaminocarbonyloxy, propylaminocarbonyloxy, isopropylaminocarbonyloxy, butylaminocarbonyloxy, tert-butylaminocarbonyloxy, pentylaminocarbonyloxy, hexylaminocarbonyloxy, dimethylaminocarbonyloxy, diethylaminocarbonyloxy, dipropylaminocarbonyloxy, dibutylaminocarbonyloxy, dipentylaminocarbonyloxy, dihexylaminocarbonyloxy, N-methyl-N-ethylaminocarbonyloxy, N-ethyl-N-propylaminocarbonyloxy, N-methyl-N-butylaminocarbonyloxy, N-methyl-N-hexylaminocarbonyloxy, and the like.

The "lower alkanoyloxy having optionally a halogen substituent" includes a straight chain or branched chain alkanoyloxy group having 1 to 6 carbon atoms which has optionally 1 to 3 substituents of a halogen atom, for example, in addition to the above lower alkanoyl group, 2,2,2-trifluoroacetyloxy, 2,2,2-trichloroacetyloxy, 2-chloroacetyloxy, 2-bromoacetyloxy, 2-fluoroacetyloxy, 2-iodoacetyloxy, 2,2-difluoroacetyloxy, 2,2-

dibromoacetyloxy, 3,3,3-trifluoropropionyloxy, 3,3,3-trichloropropionyloxy, 3-chloropropionyloxy, 2,3-dichloropropionyloxy, 4,4,4-trichlorobutyryloxy, 4-fluorobutyryloxy, 5-chloropentanoyloxy, 3-chloro-2-methylpropionyloxy, 6-bromohexanoyloxy, 5,6-dibromohexanoyloxy, and the like.

The "amino-lower alkyl having optionally a substituent selected from a lower alkyl and a lower alkanoyl" include a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents selected from a straight chain or branched chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkanoyl group having 1 to 6 carbon atoms, for example, aminomethyl, 2-aminoethyl, 1-aminoethyl, 3-aminopropyl, 4-aminobutyl, 5-aminopentyl, 6-aminohexyl, 1,1-dimethyl-2-aminoethyl, 2-methyl-3-aminopropyl, acetylaminomethyl, 1-acetylaminomethyl, 2-propionylaminomethyl, 3-isopropionylaminopropyl, 4-butyrylaminobutyl, 5-pentanoylaminopentyl, 6-hexanoylaminohexyl, formylaminomethyl, methylaminomethyl, 1-ethylaminoethyl, 2-propylaminoethyl, 3-isopropylaminopropyl, 4-butylaminobutyl, 5-pentylaminopentyl, 6-hexylaminohexyl, dimethylaminomethyl, (N-ethyl-N-propylamino)methyl, 2-(N-methyl-N-hexylamino)ethyl, and the like.

The "amino-lower alkanoyloxy having optionally a lower alkyl substituent" includes a straight chain or branched chain alkanoyloxy having 2 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms,

for example, 2-aminoacetyloxy, 3-aminopropionyloxy, 2-amino-propionyloxy, 4-aminobutyryloxy, 5-aminopentanoyloxy, 6-amino-hexanoyloxy, 2,2-dimethyl-3-aminopropionyloxy, 2-methyl-3-amino-propionyloxy, 2-methylaminoacetyloxy, 2-ethylaminopropionyloxy, 3-propylaminopropionyloxy, 3-isopropylaminopropionyloxy, 4-butyl-aminobutyryloxy, 5-pentylaminopentanoyloxy, 6-hexylaminohexanoyl-oxy, 2-dimethylaminoacetyloxy, 2-diethylaminoacetyloxy, 2-(N-ethyl-N-propylamino)acetyloxy, 3-(N-methyl-N-hexylamino)-propionyloxy, and the like.

The "pyridyl-lower alkyl" include a pyridylalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, (4-pyridyl)-methyl, 1-(3-pyridyl)ethyl, 2-(2-pyridyl)ethyl, 3-(2-pyridyl)-propyl, 4-(3-pyridyl)butyl, 5-(4-pyridyl)pentyl, 6-(2-pyridyl)-hexyl, 1,1-dimethyl-2-(3-pyridyl)ethyl, 2-methyl-3-(4-pyridyl)-propyl, and the like.

The "5- or 6-membered saturated heterocyclic group which is formed by binding the groups  $R^{82}$  and  $R^{83}$  together with the nitrogen atom to which they bond with or without being intervened with nitrogen, oxygen or sulfur atom" includes, for example, pyrrolidinyl, piperidinyl, piperazinyl, morpholino, thio-morpholino, and the like.

The above heterocyclic group which has a substituent selected from oxo, a lower alkyl, a lower alkanoyl and carbamoyl includes the above heterocyclic groups which have 1 to 3 substituents selected from oxo, a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, a straight chain or

branched chain alkanoyl group having 1 to 6 carbon atoms, and carbamoyl group, for example, 4-methylpiperazinyl, 3,4-dimethylpiperazinyl, 3-ethylpyrrolidinyl, 2-propylpyrrolidinyl, 3,4,5-trimethylpiperidinyl, 4-butylpiperidinyl, 3-pentylmorpholino, 4-hexylpiperazinyl, 2-methylthiomorpholino, 4-acetylpiperazinyl, 2-propionylmorpholino, 3-butyrylthiomorpholino, 3-pentanoylpyrrolidinyl, 4-hexanoylpiperidinyl, 3-methyl-4-acetylpiperazinyl, 2-carbamoylpyrrolidinyl, 4-carbamoylpiperazinyl, 3-carbamoylthiomorpholino, 2-carbamoylmorpholino, 3-carbamoylpiperidinyl, 1-oxo-thiomorpholino, 1,1-dioxothiomorpholino, and the like.

The "lower alkylsulfonyl" includes a straight chain or branched chain alkylsulfonyl group having 1 to 6 carbon atoms, for example, methylsulfonyl, ethylsulfonyl, propylsulfonyl, isopropylsulfonyl, butylsulfonyl, tert-butylsulfonyl, pentylsulfonyl, hexylsulfonyl, and the like.

The "aminocarbonyl having optionally a lower alkyl substituent" includes an aminocarbonyl group having optionally 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, aminocarbonyl, methylaminocarbonyl, ethylaminocarbonyl, propylaminocarbonyl, isopropylaminocarbonyl, butylaminocarbonyl, tert-butylaminocarbonyl, pentylaminocarbonyl, hexylaminocarbonyl, dimethylaminocarbonyl, diethylaminocarbonyl, dipropylaminocarbonyl, dibutylaminocarbonyl, dipentylaminocarbonyl, dihexylaminocarbonyl, N-methyl-N-ethylaminocarbonyl, N-ethyl-N-propylaminocarbonyl, N-methyl-N-butylaminocarbonyl, N-methyl-N-hexylaminocarbonyl, and the like.

The "cyano-substituted lower alkyl" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by cyano group, for example, cyanomethyl, 2-cyanoethyl, 1-cyanoethyl, 3-cyanopropyl, 4-cyanobutyl, 5-cyanopentyl, 6-cyanoethyl, 1,1-dimethyl-2-cyanoethyl, 2-methyl-3-cyanopropyl, and the like.

The "lower alkoxy-carbonyl-substituted lower alkyl" includes an alkoxy-carbonyl-substituted straight chain or branched chain alkyl group having 1 to 6 carbon atoms wherein the alkoxy-carbonyl moiety is a straight chain or branched chain alkoxy-carbonyl group having 1 to 6 carbon atoms, for example, methoxycarbonylmethyl, 3-methoxycarbonylpropyl, ethoxycarbonylmethyl, 3-ethoxycarbonylpropyl, 4-ethoxycarbonylbutyl, 5-isopropoxycarbonylpentyl, 6-propoxycarbonylhexyl, 1,1-dimethyl-2-butoxycarbonylethyl, 2-methyl-3-tert-butoxycarbonylpropyl, 2-pentyloxy-carbonylethyl, hexyloxy-carbonylmethyl, and the like.

The "carboxy-substituted lower alkyl" includes a carboxy-substituted alkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, carboxymethyl, 2-carboxyethyl, 1-carboxyethyl, 3-carboxypropyl, 4-carboxybutyl, 5-carboxypentyl, 6-carboxyhexyl, 1,1-dimethyl-2-carboxyethyl, 2-methyl-3-carboxypropyl, and the like.

The "tetrahydropyranyloxy-substituted lower alkyl" includes a tetrahydropyranyloxy-substituted straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, (2-tetrahydropyranyloxy)methyl, 2-(3-tetrahydropyranyloxy)-



oxy)ethyl, 1-(4-tetrahydropyranyloxy)ethyl, 3-(2-tetrahydro-pyranyloxy)propyl, 4-(3-tetrahydropyranyloxy)butyl, 5-(4-tetrahydropyranyloxy)pentyl, 6-(2-tetrahydropyranyloxy)hexyl, 1,1-dimethyl-2-(3-tetrahydropyranyloxy)ethyl, 2-methyl-3-(4-tetrahydropyranyloxy)propyl, and the like.

The "piperidinyl having optionally a phenyl-lower alkyl substituent" includes a piperidinyl which has optionally a substituent of a phenylalkyl group wherein the alkyl moiety is a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, piperidinyl, 1-benzyl-4-piperidinyl, 1-(2-phenylethyl)-3-piperidinyl, 1-(1-phenylethyl)-2-piperidinyl, 1-(3-phenylpropyl)-4-piperidinyl, 1-(4-phenylbutyl)-4-piperidinyl, 1-(5-phenylpentyl)-4-piperidinyl, 1-(6-phenylhexyl)-4-piperidinyl, 1-(1,1-dimethyl-2-phenylethyl)-3-piperidinyl, 1-(2-methyl-3-phenylpropyl)-2-piperidinyl, and the like.

The "imidazolyl-substituted lower alkanoyl" includes an imidazolyl-substituted alkanoyl group wherein the alkanoyl moiety is a straight chain or branched chain alkanoyl group having 2 to 6 carbon atoms, for example, (1-imidazolyl)acetyl, 3-(2-imidazolyl)propionyl, 2-(4-imidazolyl)propionyl, 4-(1-imidazolyl)butyryl, 2,2-dimethyl-3-(2-imidazolyl)propionyl, 5-(4-imidazolyl)-pentanoyl, 6-(1-imidazolyl)hexanoyl, and the like.

The "amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl" includes a straight chain or branched chain alkanoyl having 2 to 6 carbon atoms which is substituted by an amino group having optionally 1 to 2 substituents selected from a straight chain or

branch d chain alkyl group having 1 to 6 carbon atoms and a straight chain or branched chain alkoxycarbonyl group having 1 to 6 carbon atoms, for example, 2-aminoacetyl, 3-amino-propionyl, 2-aminopropionyl, 4-aminobutyryl, 5-amino-pentanoyl, 6-aminohexanoyl, 2,2-dimethyl-3-aminopropionyl, 2-methyl-3-aminopropionyl, 2-methylaminoacetyl, 2-ethyl-aminopropionyl, 3-propylaminopropionyl, 3-isopropylamino-propionyl, 4-butylaminobutyryl, 5-pentylaminopentanoyl, 6-hexylaminohexanoyl, 2-dimethylaminoacetyl, 2-diethylamino-acetyl, 2-(N-ethyl-N-propylamino)acetyl, 3-(N-methyl-N-hexylamino)propionyl, 2-methoxycarbonylaminoacetyl, 2-ethoxycarbonylaminoacetyl, 3-propoxycarbonylamino-propionyl, 4-butoxycarbonylamino-butyryl, 2-tert-butoxycarbonylamino-acetyl, 5-pentyloxycarbonylamino-pentanoyl, 6-hexyloxy-carbonylamino-hexanoyl, 2-(N-methyl-N-tert-butoxycarbonyl-amino)acetyl, and the like.

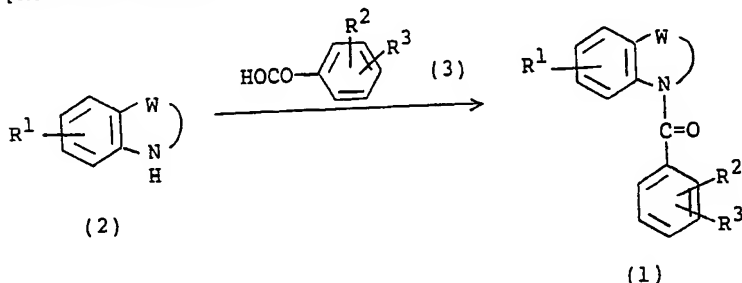
The "aminocarbonyl-lower alkyl having a lower alkyl substituent" includes a straight chain or branched chain alkyl group having 1 to 6 carbon atoms which is substituted by an aminocarbonyl group having 1 to 2 substituents of a straight chain or branched chain alkyl group having 1 to 6 carbon atoms, for example, methylaminocarbonylmethyl, 1-ethyl-aminocarbonylethyl, 2-propylaminocarbonylethyl, 3-isopropyl-aminocarbonylpropyl, 4-butylaminocarbonylbutyl, 5-pentylamino-carbonylpentyl, 6-hexylaminocarbonylhexyl, dimethylamino-carbonylmethyl, 3-diethylaminocarbonylpropyl, diethylamino-carbonylmethyl, (N-ethyl-N-propylamino)carbonylmethyl, 2-(N-

methyl-N-hexylamino)carbonylethyl, and the like.

The "amino-substituted lower alkoxy having optionally a lower alkyl substituent" includes an amino-substituted straight chain or branched chain alkoxy having 1 to 6 carbon atoms which has optionally 1 to 2 substituents of a straight chain or branched chain alkyl having 1 to 6 carbon atoms, such as aminomethoxy, 2-aminoethoxy, 1-aminoethoxy, 3-aminopropoxy, 4-aminobutoxy, 5-aminopentyloxy, 6-aminohexyloxy, 1,1-dimethyl-2-aminoethoxy, 2-methyl-3-aminopropoxy, methylaminomethoxy, 1-ethylaminoethoxy, 2-propylaminoethoxy, 3-isopropylaminopropoxy, 4-butylaminobutoxy, 5-pentylaminopentyloxy, 6-hexylaminohexyloxy, dimethylaminomethoxy, (N-ethyl-N-propylamino)methoxy, 2-(N-methyl-N-hexylamino)ethoxy, and the like.

The compounds of the present invention can be prepared by various processes, for example, by the processes shown in the following reaction schemes.

[Reaction Scheme-1]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $W$  are the same as defined above.

The process of Reaction Scheme-1 is carried out by

reacting a benzoheterocyclic compound of the formula (2) and a carboxylic acid compound of the formula (3) by a conventional amido bond forming reaction. The amido bond forming reaction can be carried out under the conditions for the conventional amido bond forming reaction, for example,

(a) a mixed acid anhydride process, i.e. a process of reacting the carboxylic acid compound (3) with an alkyl-halocarboxylic acid to form a mixed acid anhydride and reacting the resultant with the amine compound (2),

(b) an activated ester process, i.e. a process of converting the carboxylic acid compound (3) into an activated ester, such as p-nitrophenyl ester, N-hydroxy-succinimide ester, 1-hydroxybenzotriazole ester, etc., and reacting the resultant with the amine compound (2),

(c) a carbodiimide process, i.e. a process of condensing the carboxylic acid compound (3) and the amine compound (2) in the presence of an activating agent such as dicyclohexylcarbodiimide, carbonyldiimidazole, etc.,

(d) other processes, i.e. a process of converting the carboxylic acid compound (3) into a carboxylic anhydride by treatment with a dehydrating agent such as acetic anhydride, and reacting the resultant with the amine compound (2); a process of reacting an ester of the carboxylic acid compound (3) with a lower alcohol and the amine compound (2) at a high temperature under high pressure; a process of reacting an acid halide compound of the carboxylic acid compound (3), i.e. a carboxylic acid

halide, with the amine compound (2), and the like.

The mixed acid anhydride used in the above mixed acid anhydride process (a) is obtained by the known Schotten-Baumann reaction, and the reaction product is used without isolation from the reaction mixture for the reaction with the amine compound (2) to give the desired compound of the formula (1). The Schotten-Baumann reaction is usually carried out in the presence of a basic compound. The basic compound is any conventional compounds used for the Schotten-Baumann reaction and includes, for example, organic basic compounds such as triethylamine, trimethylamine, pyridine, dimethylaniline, N-methylmorpholine, 1,5-diazabicyclo[4.3.0]nonene-5 (DBN), 1,8-diazabicyclo[5.4.0]-undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), etc., and inorganic basic compounds such as potassium carbonate, sodium carbonate, potassium hydrogen carbonate, sodium hydrogen carbonate, etc. The reaction is usually carried out at a temperature of from about -20°C to about 100°C, preferably from about 0°C to about 50°C, for about 5 minutes to about 10 hours, preferably about 5 minutes to about 2 hours.

The reaction of the thus obtained mixed acid anhydride with the amine compound (2) is usually carried out at a temperature of from about -20°C to about 150°C, preferably about 10°C to about 50°C, for about 5 minutes to about 10 hours, preferably about 5 minutes to about 5 hours. The mixed acid anhydride process is usually carried

out in an appropriate solvent. The solvent is any conventional solvents which are usually used in the mixed acid anhydride process and includes, for example, halogenated hydrocarbons (e.g. chloroform, dichloromethane, dichloroethane, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. diethyl ether, diisopropyl ether, tetrahydrofuran, dimethoxyethane, etc.), esters (e.g. methyl acetate, ethyl acetate, etc.), aprotic polar solvents (e.g. N,N-dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc.), or a mixture of these solvents. The alkylhalocarboxylic acid used in the mixed acid anhydride process includes, for example, methyl chloroformate, methyl bromoformate, ethyl chloroformate, ethyl bromoformate, isobutyl chloroformate, and the like. In said process, the carboxylic acid compound (3), the alkylhalocarboxylic acid and the amine (2) are usually used in each equimolar amount, but preferably, the alkylhalocarboxylic acid and the carboxylic acid compound (3) are used each in an amount of about 1 to 1.5 mole to 1 mole of the amine (2).

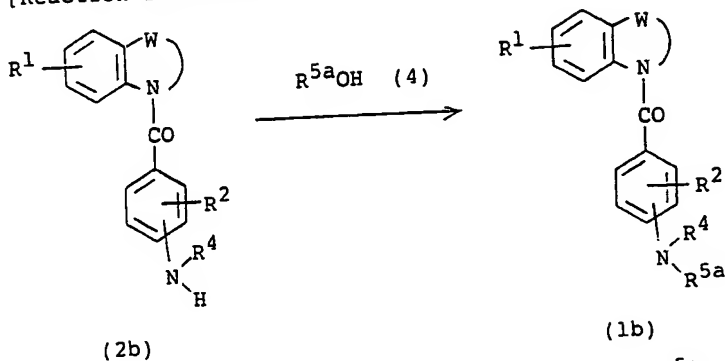
Among the above other processes (d), in case of the process of reacting the carboxylic acid halide with the amine compound (2), the reaction is usually carried out in the presence of a basic compound in an appropriate solvent. The basic compound is any conventional compounds and includes, in addition to the basic compounds used for the above-mentioned Schotten-Baumann reaction, sodium hydroxide,

potassium hydroxide, sodium hydride, potassium hydride. etc. The solvent includes, in addition to the solvents used for the above-mentioned mixed acid anhydride process, alcohols (e.g. methanol, ethanol, propanol, butanol, 3-methoxy-1-butanol, ethylcellosolve, methylcellosolve, etc.), acetonitrile, pyridine, acetone, water, and the like. The amount of the amine compound (2) and the carboxylic acid halide is not critical, but the carboxylic acid halide is usually used at least in equimolar amount, preferably about 1 to 5 moles to 1 mole of the amine compound (2). The reaction is usually carried out at a temperature of from about  $-20^{\circ}\text{C}$  to about  $180^{\circ}\text{C}$ , preferably from about  $0^{\circ}\text{C}$  to about  $150^{\circ}\text{C}$ , for about 5 minutes to about 30 hours.

The amido bond forming reaction in the above Reaction Scheme-1 may also be carried out by reacting the carboxylic acid compound (3) and the amine (2) in the presence of a condensation agent, i.e. phosphoric compounds such as triphenylphosphine, diphenylphosphinyl chloride, phenyl-N-phenylphosphoramidate chloridate, diethyl chlorophosphate, diethyl phosphorocyanidate, diphenylphosphoric azide, bis(2-oxo-3-oxazolidinyl)phosphinic chloride, etc. The reaction is usually carried out in the presence of the solvent and basic compound as used in the above reaction of the carboxylic acid halide and the amine (2) at a temperature of from about  $-20^{\circ}\text{C}$  to about  $150^{\circ}\text{C}$ , preferably about  $0^{\circ}\text{C}$  to about  $100^{\circ}\text{C}$ , for about 5 minutes to about 30 hours. The condensation agent and the carboxylic acid compound (3)

are used at least in equimolar amount, preferably about 1 to 2 moles, to 1 mole of the amine (2).

[Reaction Scheme-2]

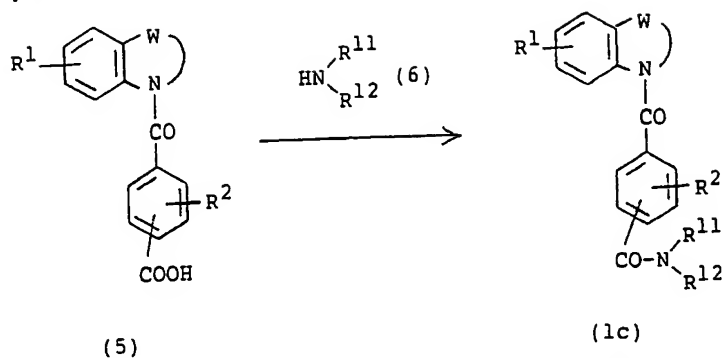


wherein  $R^1$ ,  $R^2$ ,  $R^4$  and  $W$  are as defined above,  $R^{5a}$  is the same as  $R^5$  as defined above except excluding an anilino-carbonyl having optionally a lower alkyl substituent on the phenyl ring, a phenylsulfonyl having optionally a substituent selected from a halogen atom and a lower alkyl on the phenyl ring and quinolylsulfonyl.

The reaction of the compound (2b) and the compound (4) is carried out in the same manner as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.



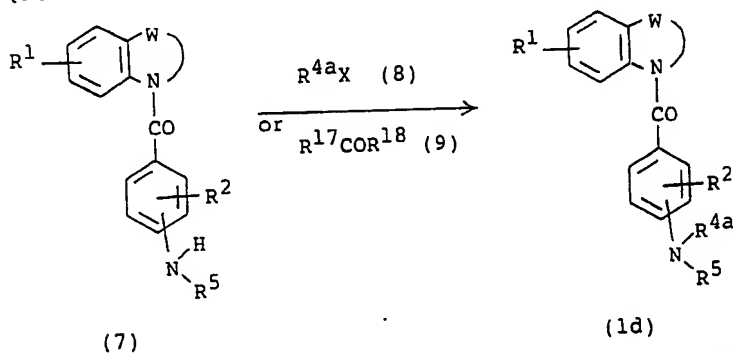
## [Reaction Scheme-3]



wherein  $R^1$ ,  $R^2$ ,  $R^{11}$ ,  $R^{12}$  and  $W$  are as defined above.

The reaction of the compound (5) and the compound (6) is carried out under the same conditions as used in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

## [Reaction Scheme-4]



wherein  $R^1$ ,  $R^2$ ,  $R^5$  and  $W$  are as defined above, and  $R^{4a}$  is a lower alkyl,  $R^{17}$  and  $R^{18}$  are each hydrogen atom or a lower alkyl, and  $X$  is a halogen atom.

The reaction of the compound (7) and the compound (8) is usually carried out in an inert solvent in the

presence or absence of a basic compound. The inert solvent includes, for example, aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. tetrahydrofuran, dioxane, diethylene glycol dimethyl ether, etc.), halogenated hydrocarbons (e.g. dichloromethane, chloroform, carbon tetrachloride, etc.), lower alcohols (e.g. methanol, ethanol, isopropanol, butanol, tert-butanol, etc.), acetic acid, ethyl acetate, acetone, acetonitrile, pyridine, dimethylsulfoxide, dimethylformamide, hexamethylphosphoric triamide, etc., or a mixture of these solvents. The basic compound includes, for example, carbonates (e.g. sodium carbonate, potassium carbonate, sodium hydrogen carbonate, potassium hydrogen carbonate, etc.), metal hydroxides (e.g. sodium hydroxide, potassium hydroxide, etc.), sodium hydride, potassium, sodium, sodium amide, metal alcoholates (e.g. sodium methoxide, sodium ethoxide, etc.), and organic basic compounds (e.g. pyridine, N-ethyldiisopropylamine, dimethylaminopyridine, triethylamine, 1,5-diazabicyclo-[4.3.0]nonene-(5) (DBN), 1,8-diazabicyclo[5.4.0]undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), etc.). The amount of the compound (7) and the compound (8) is not critical, but the compound (8) is usually used at least in equivalent amount, preferably 1 to 10 moles, to 1 mole of the compound (7). The reaction is usually carried out at a temperature of from about 0°C to about 200°C, preferably from about 0°C to about 170°C, for about 30 minutes to about 30 hours. In the reaction, an alkali metal halide (e.g.

sodium iodide, potassium iodide, etc.) may be added to the reaction system.

The reaction of the compound (7) and the compound (9) is carried out in an appropriate solvent or without solvent in the presence of a reducing agent. The solvent includes, for example, water, alcohols (e.g. methanol, ethanol, isopropanol, etc.), acetonitrile, formic acid, acetic acid, ethers (e.g. dioxane, diethyl ether, diglyme, tetrahydrofuran, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), or a mixture of these solvents. The reducing agent includes, for example, formic acid, fatty acid alkali metal salts (e.g. sodium formate, etc.), hydrogenating reducing agents (e.g. sodium borohydride, sodium cyanoborohydride, lithium aluminum hydride, etc.), catalytic reducing agents (e.g. palladium black, palladium-carbon, platinum oxide, platinum black, Raney nickel, etc.).

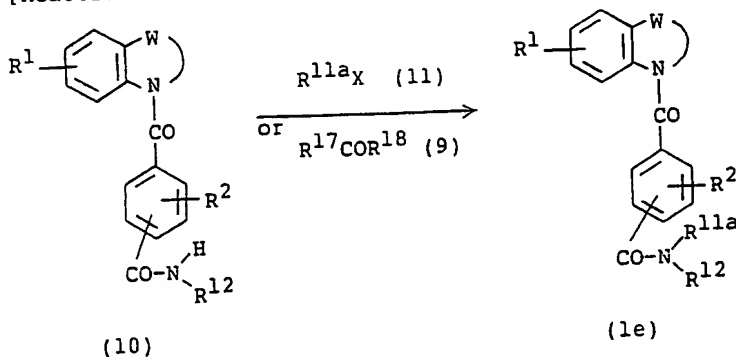
When formic acid is used as the reducing agent, the reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably about 50°C to about 150°C, for about 1 to 10 hours. The formic acid is usually used in a large excess amount to the compound (7).

When a hydrogenating reducing agent is used, the reaction is usually carried out at a temperature of about -30°C to about 100°C, preferably about 0°C to about 70°C, for about 30 minutes to about 12 hours. The reducing agent is usually used in an amount of 1 to 20 moles, preferably 1

to 6 moles, to 1 mole of the compound (7). When lithium aluminum hydride is used as the reducing agent, it is preferable to use a solvent selected from ethers (e.g. diethyl ether, dioxane, tetrahydrofuran, diglyme, etc.) and aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.).

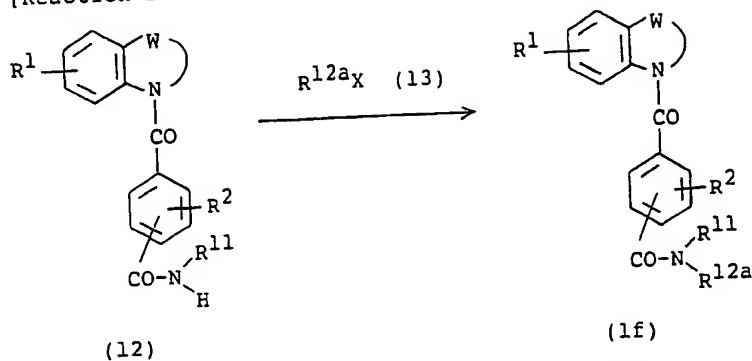
When a catalytic reducing agent is used, the reaction is usually carried out under atmospheric pressure to about 20 atm., preferably atmospheric pressure to about 10 atm. under hydrogen atmosphere or in the presence of a hydrogen donor (e.g. formic acid, ammonium formate, cyclohexene, hydrazine hydrate, etc.) at a temperature of about  $-30^{\circ}\text{C}$  to about  $100^{\circ}\text{C}$ , preferably about  $0^{\circ}\text{C}$  to about  $60^{\circ}\text{C}$ , for about 1 to 12 hours. The catalytic reducing agent is usually used in an amount of about 0.1 to 40 % by weight, preferably about 1 to 20 % by weight, of the amount of the compound (7). The compound (9) is usually used at least in equivalent amount, preferably equivalent to a large excess amount, to the compound (7).

[Reaction Scheme-5A]



wherein  $R^1$ ,  $R^2$ ,  $R^{12}$ ,  $R^{17}$ ,  $R^{18}$ ,  $X$  and  $W$  are as defined above, and  $R^{11a}$  is a lower alkyl.

[Reaction Scheme-5B]

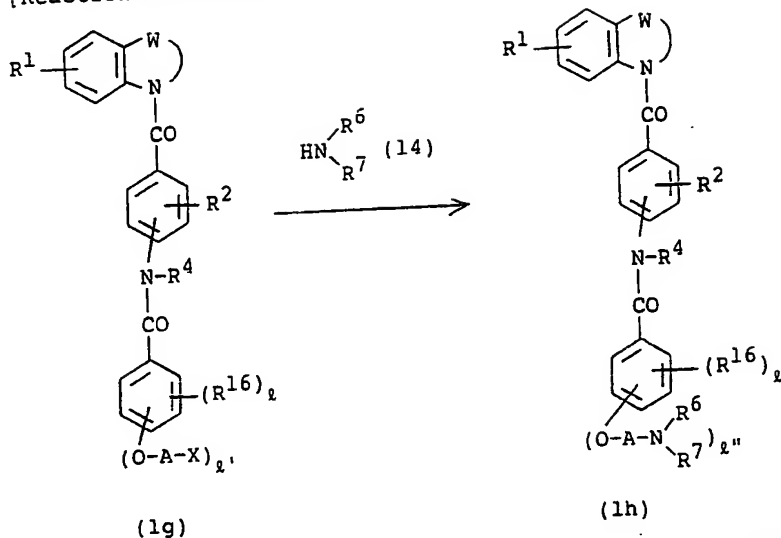


wherein  $R^1$ ,  $R^2$ ,  $R^{11}$ ,  $X$  and  $W$  are as defined above, and  $R^{12a}$  is a cycloalkyl.

The reaction of the compound (10) and the compound (11) in the Reaction Scheme-5A and the reaction of the compound (12) and the compound (13) in the Reaction Scheme-5B are carried out in the same manner as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

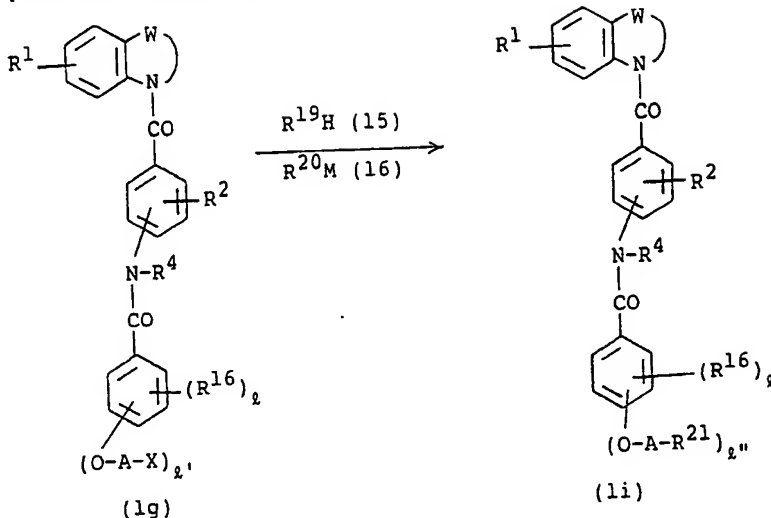
Besides, the reaction of the compound (10) and the compound (9) in the Reaction Scheme-5A is carried out in the same manner as in the reaction of the compound (7) and the compound (9) in the above Reaction Scheme-4.

[Reaction Scheme-6A]



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^4$ ,  $\text{R}^{16}$ ,  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{X}$ ,  $\text{W}$ , and  $\text{A}$  are as defined above,  $\text{z}$  is 0 or an integer of 1 to 3,  $\text{z}'$  and  $\text{z}''$  are each an integer of 1 to 3, provided that  $\text{z} + \text{z}'$  and  $\text{z} + \text{z}''$  are each an integer not more than 3.

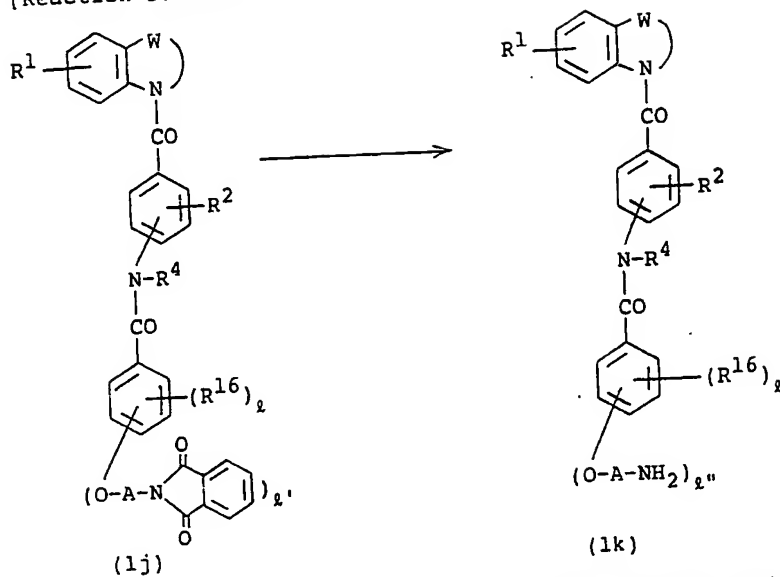
[Reaction Scheme-6B]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $X$ ,  $W$ ,  $A$ ,  $\ell$ ,  $\ell'$ , and  $\ell''$  are as defined above, and  $R^{19}$  is a lower alkanoyloxy,  $R^{20}$  is a lower alkanoyloxy, hydroxy or phthalimido,  $R^{21}$  is the same as as  $R^{19}$  and  $R^{20}$ , and  $M$  is an alkali metal (e.g. potassium, sodium, etc.).

The reaction of the compound (1g) and the compound (14) in the Reaction Scheme-6A and the reaction of the compound (1g) and the compound (15) or (16) in the Reaction Scheme-6B can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be added to the reaction system.

[Reaction Scheme-7]



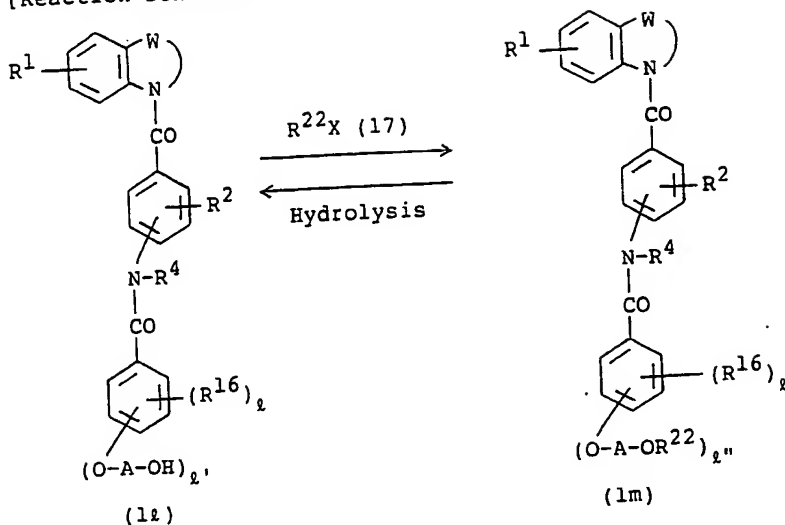
wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $W$ ,  $l$ ,  $l'$ ,  $l''$  and  $A$  are as defined above.

The reaction of converting the compound (1j) into the compound (1k) can be carried out by reacting the compound (1j) with hydrazine in an appropriate solvent or by hydrolyzing the compound (1j). The solvent used in the reaction with hydrazine includes water and further the same solvent as used in the reaction of the compound (2b) and the compound (4) in the above Reaction Scheme-2. The reaction is usually carried out at a temperature of from room temperature to about 120°C, preferably about 0°C to about 100°C, for about 0.5 to 5 hours. Hydrazine is usually used in an amount of at least 1 mole, preferably about 1 to 5 moles, to 1 mole of the compound (1j).



The hydrolysis can be carried out in an appropriate solvent or without solvent in the presence of an acid or a basic compound. The solvent includes, for example, water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ketones (e.g. acetone, methyl ethyl ketone, etc.), ethers (e.g. dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, etc.), fatty acids (e.g. acetic acid, formic acid, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, sulfuric acid, hydrobromic acid, etc.) and organic acids (e.g. formic acid, acetic acid, aromatic sulfonic acids, etc.). The basic compound includes, for example, metal carbonates (e.g. sodium carbonate, potassium carbonate, etc.), metal hydroxides (e.g. sodium hydroxide, potassium hydroxide, calcium hydroxide, etc.), and the like. The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 10 minutes to 25 hours.

[Reaction Scheme-8]

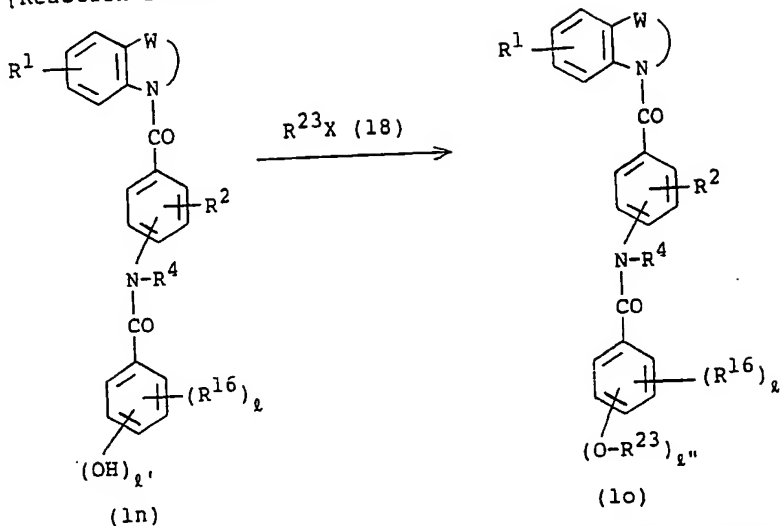


wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ ,  $R^{16}$ ,  $z$ ,  $z'$ ,  $z''$ ,  $X$ , and  $A$  are as defined above, and  $R^{22}$  is a lower alkanoyl.

The reaction of the compound (1l) and the compound (17) is carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be added to the reaction system.

The reaction of converting the compound (1m) into the compound (1l) can be carried out under the same condition as in the hydrolysis of the compound (1j) in the Reaction Scheme-7.

[Reaction Scheme-9]

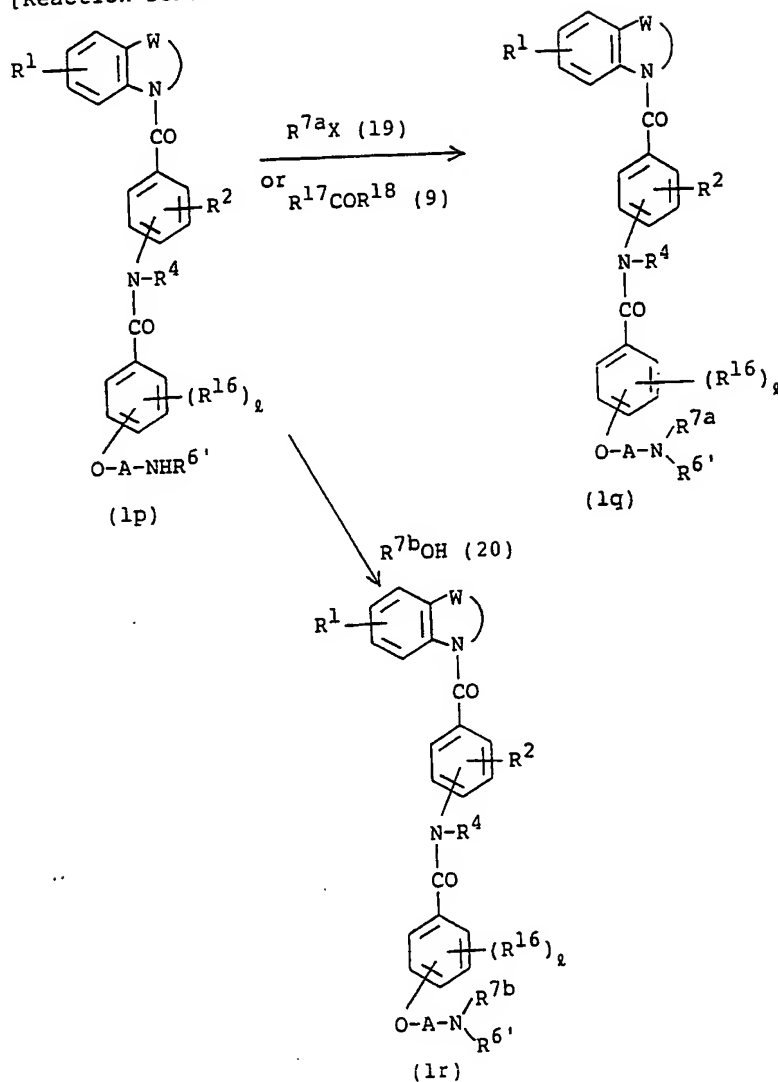


wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ ,  $R^{16}$ ,  $2$ ,  $2'$ ,  $2''$ , and  $X$  are as defined above, and  $R^{23}$  is a lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a halogen-substituted lower alkyl, a carboxy-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a hydroxy-substituted lower alkyl, a lower alkoxy-carbonyl-substituted lower alkyl, a phthalimido-substituted lower alkyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a group of the formula:  $-\text{A}-\text{N} \begin{smallmatrix} \text{R}^6 \\ \text{R}^7 \end{smallmatrix}$  ( $A$ ,  $R^6$  and  $R^7$  are as defined above).

The reaction of the compound (1n) and the compound (18) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be

added to the reaction system.

[Reaction Scheme-10]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$ ,  $\epsilon$ ,  $X$ , and  $A$  are as defined above, and  $R^{6'}$  is hydrogen atom, a lower alkyl

having optionally a hydroxy substituent, a lower alkanoyl, or benzoyl,  $R^{7a}$  is a lower alkyl having optionally a hydroxy substituent, and  $R^{7b}$  is a lower alkanoyl or benzoyl.

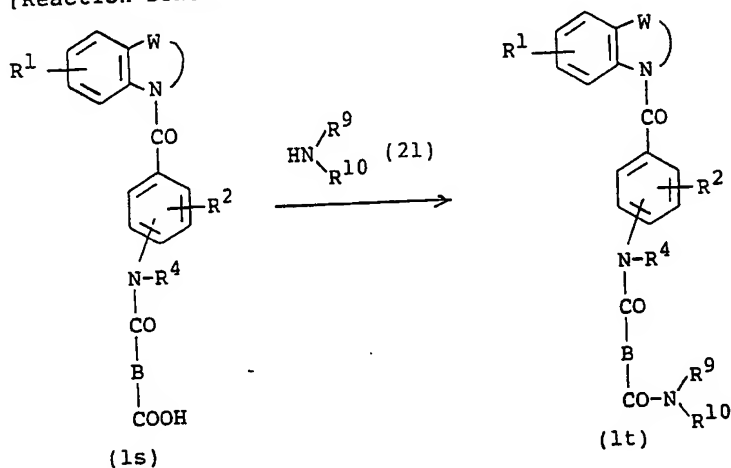
The reaction of the compound (1p) and the compound (19) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1p) and the compound (20) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the Reaction Scheme-1.

Besides, the compound (1r) can also be obtained by reacting the compound (1p) with a compound of the formula:  $(R^{7b})_2O$  ( $R^{7b}$  is as defined above). The reaction can be carried out in an appropriate solvent or without solvent in the presence or absence, preferably presence, of a basic compound. The solvent includes, for example, the above-mentioned aromatic hydrocarbons, lower alcohols (e.g. methanol, ethanol, propanol, etc.), dimethylformamide, dimethylsulfoxide, and further halogenated hydrocarbons (e.g. chloroform, methylene chloride, etc.), acetone, pyridine, etc. The basic compound includes, for example, tertiary amines (e.g. triethylamine, pyridine, etc.), sodium hydroxide, potassium hydroxide, sodium hydride, and the like. The above reaction can also be carried out in a solvent such as acetic acid or benzoic acid in the presence of a mineral acid (e.g. sulfuric acid, etc.). The acid

anhydride is usually used in an equimolar amount or more, preferably 1 to 10 moles, to 1 mole of the starting compound, and the reaction is usually carried out at a temperature of about 0°C to about 200°C, preferably from about 0°C to about 150°C, for about 0.5 to 15 hours.

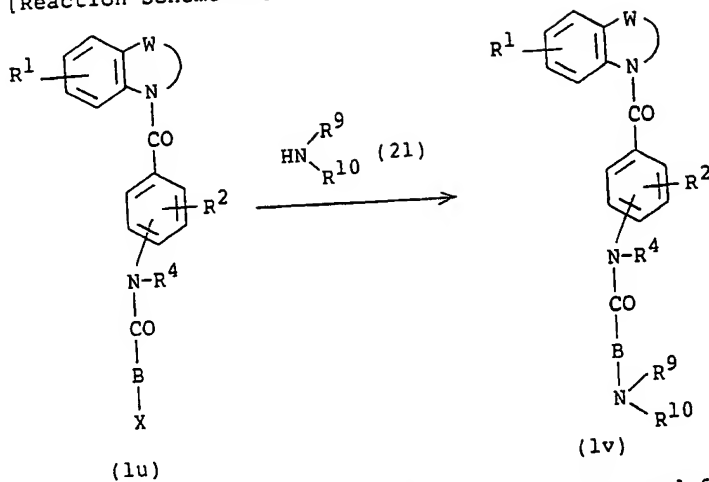
[Reaction Scheme-11]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^9$ ,  $R^{10}$ ,  $W$ , and  $B$  are as defined above.

The reaction of the compound (1s) and the compound (21) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

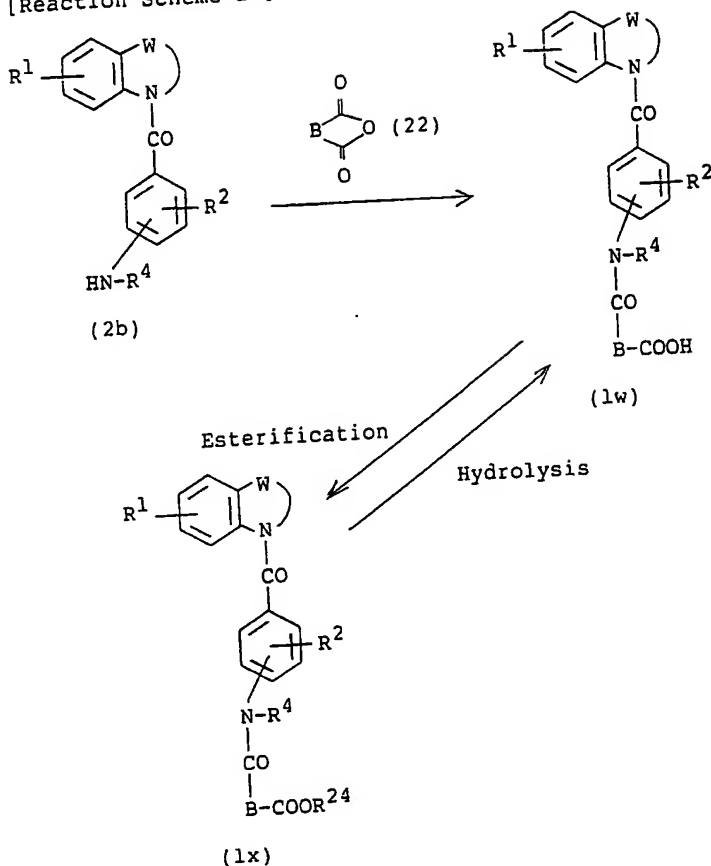
[Reaction Scheme-12]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ ,  $R^9$ ,  $R^{10}$ ,  $X$ , and  $B$  are as defined above.

The reaction of the compound (1u) and the compound (21) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. In the reaction, an alkali metal halide (e.g. sodium iodide, potassium iodide, etc.) may be added to the reaction system.

[Reaction Scheme-13]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ , and  $B$  are as defined above, and  $R^{24}$  is a lower alkyl.

The reaction of the compound (2b) and the compound (22) can be carried out in an appropriate inert solvent. The inert solvent includes, for example, aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. tetrahydrofuran, dioxane, diethylene glycol dimethyl

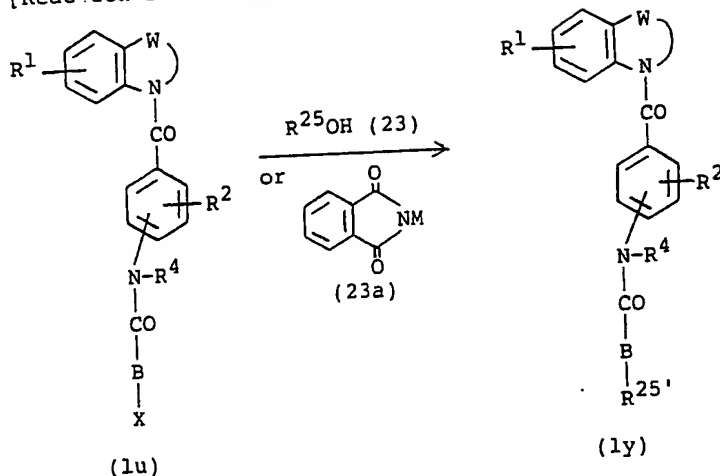


ether, etc.), lower alcohols (e.g. methanol, ethanol, isopropanol, butanol, etc.), halogenated hydrocarbons (e.g. dichloromethane, chloroform, carbon tetrachloride, etc.), acetic acid, ethyl acetate, acetonitrile, dimethylsulfoxide, dimethylformamide, hexamethylphosphoric triamide, and the like. The amount of the compound (2b) and the compound (22) is not critical, but the compound (22) is usually used in an amount of at least one mole, preferably 1 to 2 moles, to 1 mole of the compound (2b). The reaction is usually carried out at a temperature of from about 0°C to about 150°C, preferably from about 0°C to about 100°C, for about 30 minutes to about 10 hours.

The esterification of the compound (1w) is usually carried out by reacting the starting compound with an alcohol (e.g. methanol, ethanol, isopropanol, etc.) in the presence of a mineral acid (e.g. hydrochloric acid, sulfuric acid, etc.) and a halogenating agent (e.g. thionyl chloride, phosphorus oxychloride, phosphorus pentachloride, phosphorus trichloride, etc.) at a temperature of 0°C to 150°C, preferably 50°C to 100°C, for about 1 to 10 hours.

The hydrolysis of the compound (1x) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the Reaction Scheme-7.

[Reaction Scheme-14]



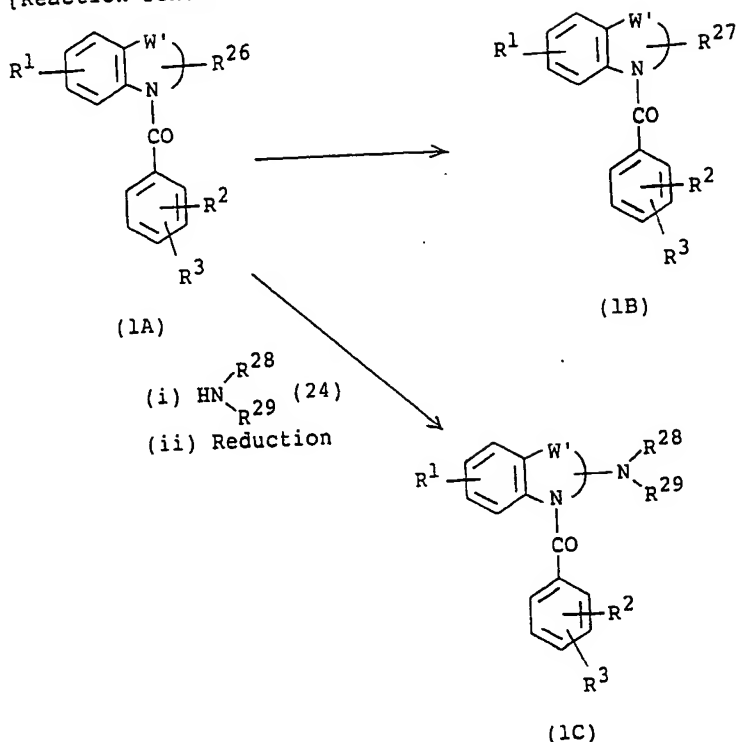
wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ ,  $B$ ,  $M$ , and  $X$  are as defined above, and  $R^{25}$  is a phenyl which has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent, or naphthyl, and  $R^{25'}$  is a phenoxy which has optionally 1 to 3 substituents selected from a lower alkyl, a lower alkoxy and an amino having optionally a lower alkanoyl substituent, naphthyloxy or phthalimido.

The reaction of the compound (1u) and the compound (23) or (23a) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The compound (1y) wherein  $R^{25'}$  is phthalimido can be converted into the compound (1y) wherein  $R^{25'}$  is amino under the same conditions as in the reaction of converting the compound (1j) into the compound (1k) in the above

## Reaction Scheme-7.

[Reaction Scheme-15]



wherein  $R^1$ ,  $R^2$  and  $R^3$  are as defined above, and  $R^{26}$  is oxo,  $R^{27}$  is hydroxy, and  $W'$  is the same as  $W$ , provided that the substituents on the group  $-(CH_2)_p-$  or  $-CH=CH-(CH_2)_q-$  are 0 to 2, and  $R^{28}$  and  $R^{29}$  are the same or different and are each hydrogen atom, a lower alkenyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a cyano-substituted

lower alkyl, a lower alkoxy carbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl which has optionally a phenyl-lower alkyl substituent, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a lower alkyl, or  $R^{28}$  and  $R^{29}$  may bind together with the nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom, which heterocyclic ring may optionally have a substituent selected from a lower alkyl, a phenyl-lower alkyl, or a lower alkanoyl.

The conversion of the compound (1A) into the compound (1B) is carried out by reduction thereof. The reducing reaction is preferably carried out by using a hydrogenating reducing agent (e.g. lithium aluminum hydride, sodium boro hydride, diborane, etc.). The reducing agent is usually used in an amount of at least one mole, preferably 1 to 15 moles, to 1 mole of the starting compound. The reducing reaction is usually carried out in an appropriate solvent, for example, water, alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diisopropyl ether, diglyme, etc.), or a mixture of these solvents, at a temperature of from about  $-60^{\circ}\text{C}$  to about  $150^{\circ}\text{C}$ , preferably about  $-30^{\circ}\text{C}$  to about  $100^{\circ}\text{C}$ , for about 10 minutes to 15 hours. When lithium aluminum

hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as tetrahydrofuran, diethyl ether, diisopropyl ether, diglyme, etc.

The reaction of converting the compound (1A) into the compound (1C) is usually carried out in an appropriate solvent or without solvent in the presence or absence of a dehydrating agent. The solvent includes, for example, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), halogenated hydrocarbons (e.g. dichloromethane, dichloroethane, chloroform, carbon tetrachloride, etc.), aprotic polar solvents (e.g. dimethylformamide, dimethylacetamide, N-methylpyrrolidone, etc.), or a mixture of these solvents. The dehydrating agent includes, for example, conventional drying agent used for dehydrating solvents (e.g. molecular sieves, etc.), mineral acids (e.g. hydrochloric acid, sulfuric acid, borane trifluoride, etc.), organic acids (e.g. p-toluenesulfonic acid, etc.), and the like. The reaction is usually carried out at a temperature of from room temperature to about 250°C, preferably from about 50°C to about 200°C, for about 1 to 48 hours. The amount of the compound (24) is not critical, but it is usually used at least in an equivalent amount, preferably equimolar to largely excess to the amount of the compound (1A). The dehydrating agent is preferably used in a largely excess amount in case of the drying agent and in a catalytic amount in case of the acid.

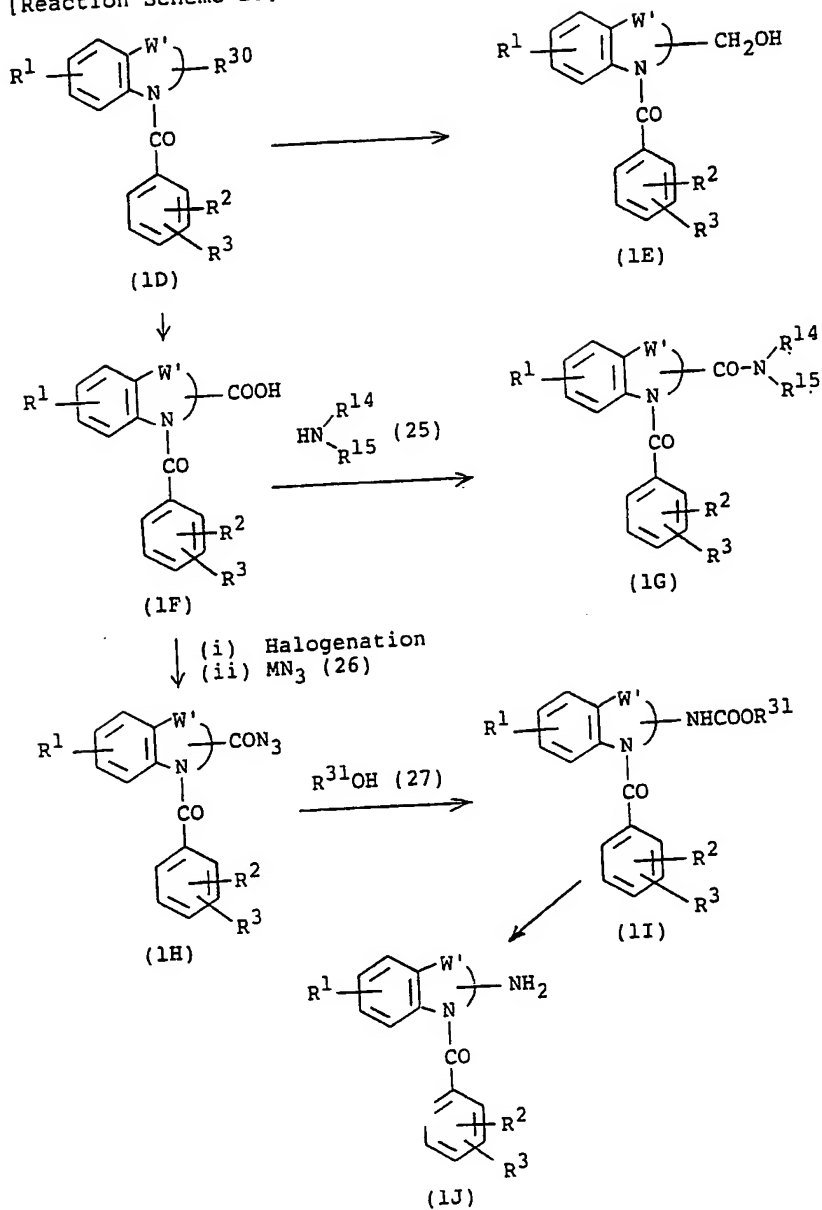
The subsequent reducing reaction can be carried out by various methods, for example by catalytically hydrogenating the compound in an appropriate solvent in the presence of a catalyst. The solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. diethylene glycol dimethyl ether, dioxane, tetrahydrofuran, diethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.), aprotic polar solvents (e.g. dimethylformamide, etc.), or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the starting compound. The reaction is usually carried out at a temperature of from about -20°C to about 100°C, preferably about 0°C to about 70°C, under a hydrogen atmospheric pressure of 1 to 10 atm. for about 0.5 to 20 hours.

Although the reducing reaction can be carried out under the above conditions, it is preferably carried out by using a hydrogenating reducing agent. The hydrogenating reducing agent includes, for example, lithium aluminum hydride, sodium borohydride, diborane, etc., and it is usually used in an amount of at least one mole, preferably 1 to 10 moles, to 1 mole of the compound (1A). The reaction is usually carried out in an appropriate solvent, such as

water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diglyme, etc.), dimethylformamide, or a mixture of these solvents, at a temperature of about  $-60^{\circ}\text{C}$  to about  $50^{\circ}\text{C}$ , preferably about  $-30^{\circ}\text{C}$  to room temperature, for about 10 minutes to about 5 hours. When lithium aluminum hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as diethyl ether, tetrahydrofuran, diglyme, etc.

The compound (1C) wherein at least one of  $\text{R}^{28}$  and  $\text{R}^{29}$  is hydrogen atom can be converted into the compound (1C) wherein at least one of  $\text{R}^{28}$  and  $\text{R}^{29}$  is a lower alkyl by reacting the compound (1C) with the compound (8) or the compound (9) under the same conditions as in the reaction of the compound (7) and the compound (8) or (9) in the above Reaction Scheme-4.

[Reaction Scheme-16]





wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^{14}$ ,  $R^{15}$ ,  $W'$ , and  $M$  are as defined above, and  $R^{31}$  is a phenyl-lower alkyl, and  $R^{30}$  is a lower alkoxy carbonyl.

The reaction of converting the compound (1D) into the compound (1E) can be carried out under the same conditions as in the reaction of converting the compound (1A) into the compound (1B) in the above Reaction Scheme-15.

The reaction of converting the compound (1D) into the compound (1F) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1j) in the above Reaction Scheme-7.

The reaction of the compound (1F) and the compound (25) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The halogenation of the compound (1F) can be carried out under a conventional condition for halogenation of a carboxylic acid. The reaction of the thus-obtained carboxylic acid halide of the compound (1F) with the compound (26) is carried out in an appropriate solvent in the presence or absence of a basic compound. The solvent includes, for example, halogenated hydrocarbons (e.g. methylene chloride, chloroform, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), ethers (e.g. diethyl ether, tetrahydrofuran, dimethoxyethane, etc.), esters (e.g. methyl acetate, ethyl acetate, etc.), aprotic polar solvents

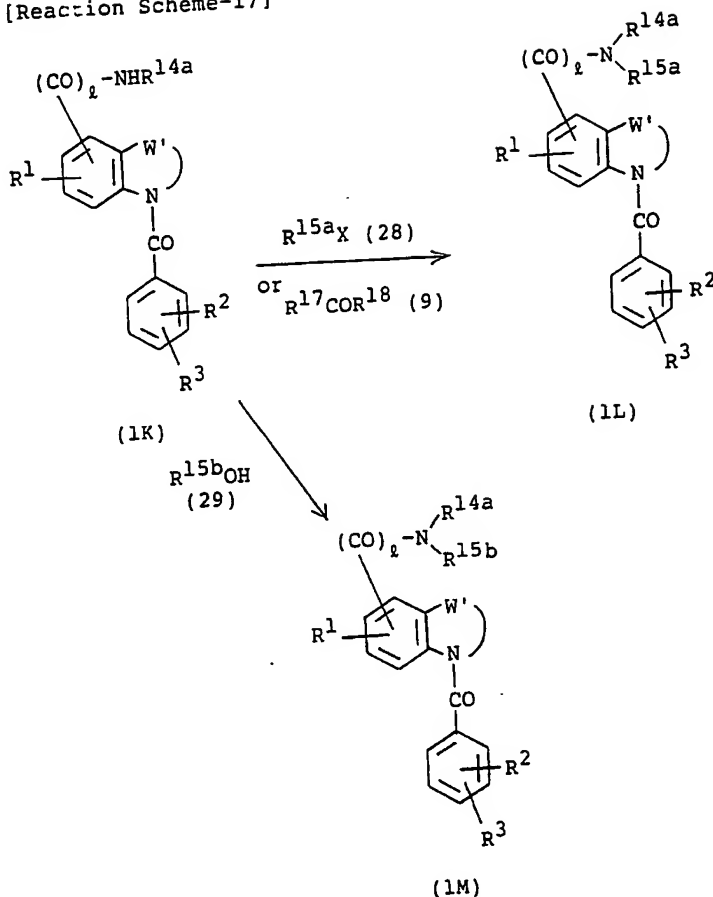
(e.g. N,N-dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc.), alcohols (e.g. methanol, ethanol, propanol, butanol, 3-methoxy-1-butanol, ethyl cellosolve, methyl cellosolve, etc.), pyridine, acetone, acetonitrile, water, or a mixture of these solvents. The basic compound includes, for example, organic bases such as triethylamine, trimethylamine, pyridine, dimethylaniline, N-methylmorpholine, DBN, DBU, DABCO, etc., inorganic bases such as potassium carbonate, sodium carbonate, potassium hydroxide, sodium hydroxide, potassium hydride, sodium hydride, silver carbonate, alcoholates (e.g. sodium methylate, sodium ethylate, etc.), and the like. The compound (26) is usually used in an amount of at least 1 mole, preferably 1 to 1.5 mole, to 1 mole of the carboxylic acid halide of the compound (1F). The reaction is usually carried out at a temperature of from  $-30^{\circ}\text{C}$  to about  $180^{\circ}\text{C}$ , preferably from about  $0^{\circ}\text{C}$  to about  $150^{\circ}\text{C}$ , for about 5 minutes to 30 hours.

The reaction of the compound (1H) and the compound (27) is carried out in an appropriate solvent or without solvent at a temperature of from about  $0^{\circ}\text{C}$  to about  $200^{\circ}\text{C}$ , preferably from room temperature to about  $150^{\circ}\text{C}$ . The solvent includes the same solvents as used in the above reaction of the carboxylic acid halide of the compound (1F) and the compound (26). The compound (27) is preferably used in an amount largely excess to the the compound (1H). The reaction is usually completed in a reaction time of about 1

to 5 hours.

The reaction of converting the compound (1I) into the compound (1J) can be carried out by reducing the compound. The reducing reaction is usually carried out by catalytically hydrogenating the compound in an appropriate solvent in the presence of a catalyst. The solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.), aprotic polar solvents (e.g. N,N-dimethylformamide, etc.), acetic acid, or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the starting compound. The reaction is usually carried out at a temperature of from about -20°C to about 100°C, preferably about 0°C to about 80°C, under a hydrogen atmospheric pressure of 1 to 10 atm. for about 0.5 to 20 hours.

[Reaction Scheme-17]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $\ell$ ,  $R^{17}$ ,  $R^{18}$ , and  $X$  are as defined above, and  $R^{14a}$  is hydrogen atom, a lower alkyl, a lower alkanoyl, a lower alkenyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl,

benzoyl, a lower alkoxy-carbonyl, anilinocarbonyl, an amino-carbonyl having optionally a lower alkyl substituent, a cyano-substituted lower alkyl, a lower alkoxy-carbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent, a halogen-substituted lower alkanoyl, an imiazolyl-substituted lower alkanoyl, an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxy-carbonyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a phenyl-lower alkoxy-carbonyl,  $R^{15a}$  is a lower alkyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl, a cyano-substituted lower alkyl, a lower alkoxy-carbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyloxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a lower alkenyl, and  $R^{15b}$  is a lower alkanoyl, a phenyl-lower alkoxy-carbonyl, benzoyl, a lower alkoxy-carbonyl, a halogen-substituted lower alkanoyl, an

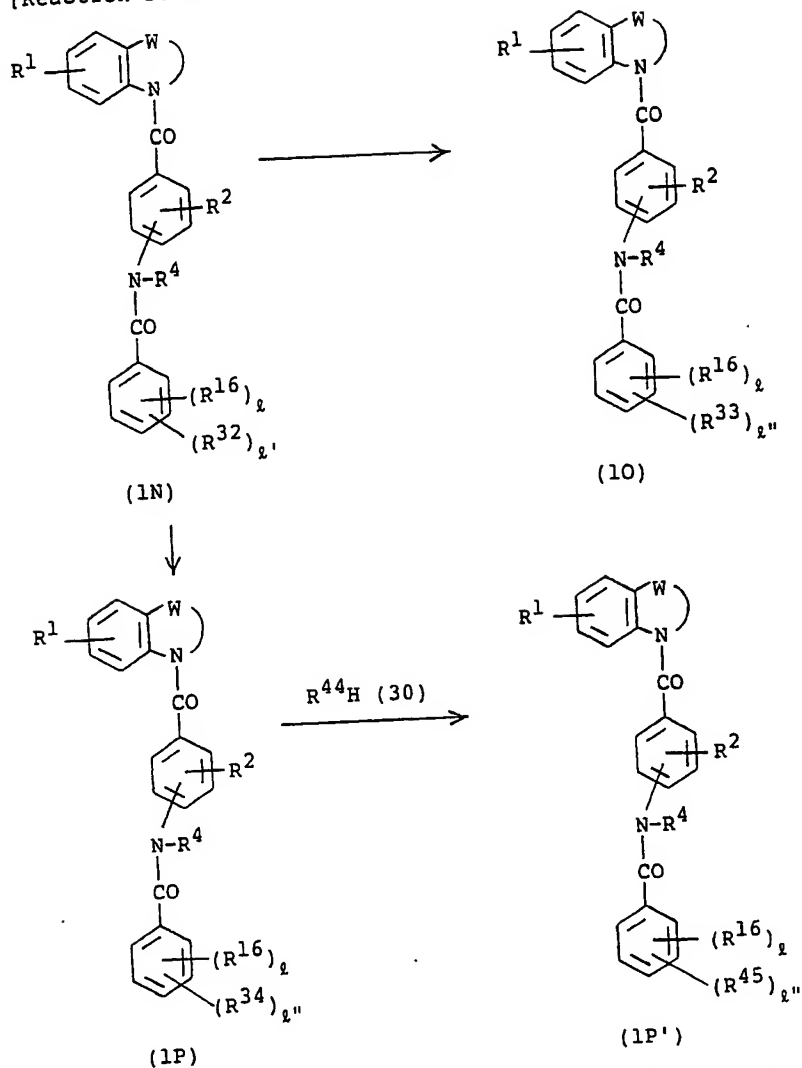
imidazolyl-substituted lower alkanoyl, or an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxy carbonyl.

The reaction of the compound (1K) and the compound (28) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1K) and the compound (29) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1. The compound (1M) can also be obtained by reacting the compound (1K) with a compound of the formula  $(R^{15b})_2O$  (wherein  $R^{15b}$  is as defined above). The reaction can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula:  $(R^{7b})_2O$  as described hereinbefore.

The compound (1M) wherein  $R^{15b}$  is formyl can also be prepared by reacting the compound (1K) with a formate of the formula:  $HCOOR^{82}$  ( $R^{82}$  is a lower alkyl). The reaction is usually carried out in the solvent as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4 or without solvent, at a temperature of about  $0^{\circ}C$  to about  $200^{\circ}C$ , preferably about  $0^{\circ}C$  to about  $170^{\circ}C$ , for about 30 minutes to about 30 hours. The formate is preferably used in a largely excess amount to the compound (1K).

[Reaction Scheme-18]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $W$ ,  $2$ ,  $2'$  and  $2''$  are as defined above, and  $R^{32}$  is a lower alkoxy-carbonyl-substituted lower alkoxy,  $R^{33}$  is a carbamoyl-substituted lower alkoxy,  $R^{34}$  is

a carboxy-substituted lower alkoxy,  $R^{44}$  is an amino having optionally a lower alkyl substituent, and  $R^{45}$  is an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent.

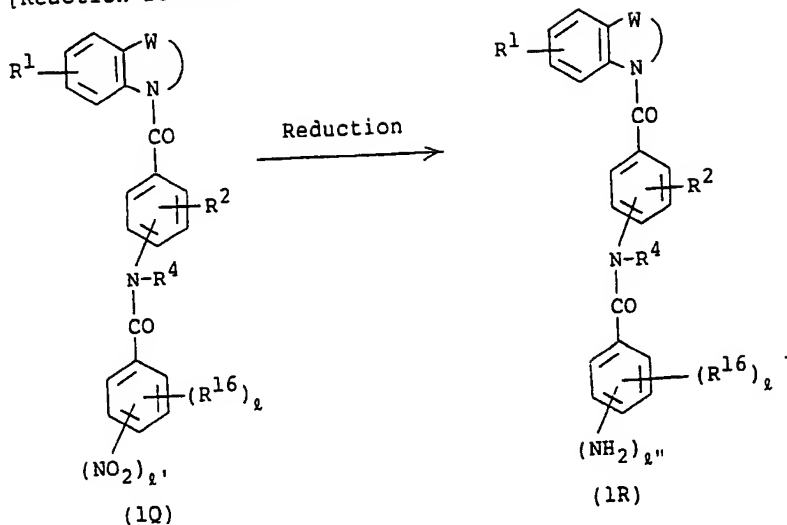
The conversion of the compound (1N) into the compound (1O) can be carried out by reacting the compound with aqueous ammonia in an appropriate solvent in an autoclave. The solvent includes the same solvents as used in the reaction of the carboxylic acid halide and the amine (2) in the above Reaction Scheme-1. The aqueous ammonia is used in a largely excess amount to the compound (1N). The reaction proceeds advantageously by adding an ammonium halide (e.g. ammonium chloride, etc.) to the reaction system. The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 1 to 10 hours.

The reaction of converting the compound (1N) into the compound (1P) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the above Reaction Scheme-7.

The reaction of the compound (1P) and the compound (30) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.



[Reaction Scheme-19]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $W$ ,  $l$ ,  $l'$  and  $l''$  are as defined above.

The reducing reaction in the above reaction scheme is usually carried out, for example, (i) with a reducing catalyst in an appropriate solvent or (ii) with a reducing agent such as a mixture of a metal or metal salt with an acid, or a mixture of a metal or metal salt with an alkali metal hydroxide, a sulfide or an ammonium salt in an appropriate inert solvent.

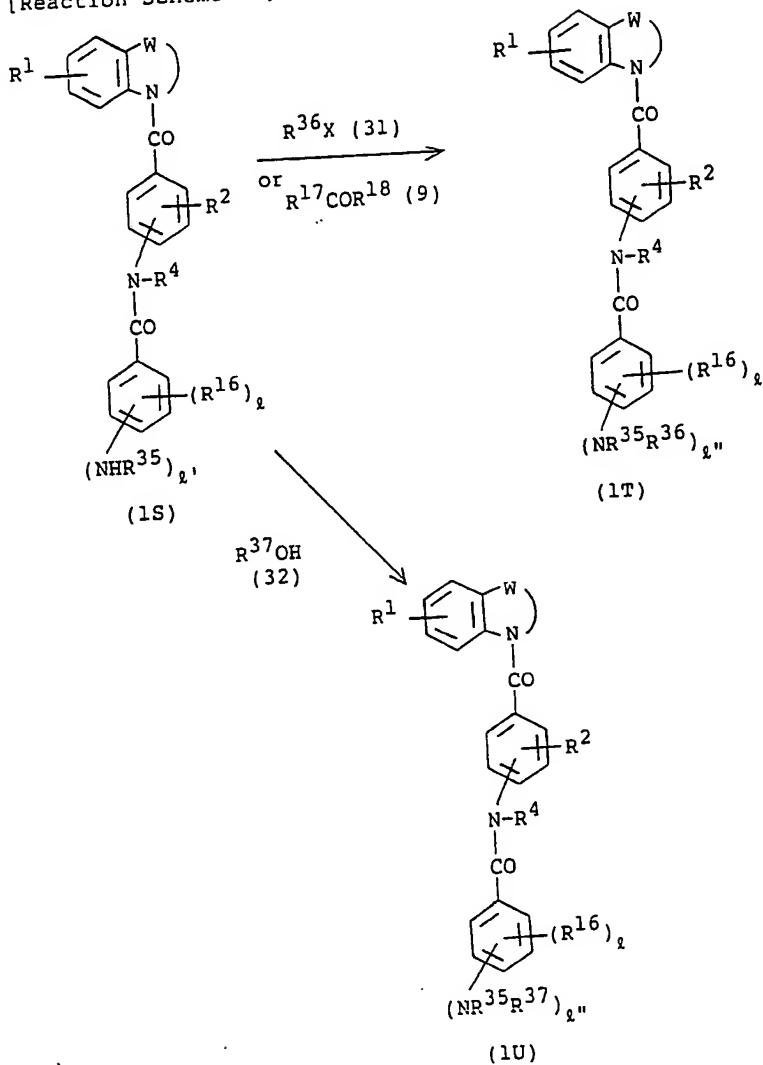
In case of using a reducing catalyst, the solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, diethylene glycol dimethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.),

aprotic polar solvents (e.g. N,N-dimethylformamide, etc.), or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromite, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the starting compound. The reaction is usually carried out at a temperature of from about  $-20^{\circ}\text{C}$  to about  $150^{\circ}\text{C}$ , preferably about  $0^{\circ}\text{C}$  to about  $100^{\circ}\text{C}$ , under a hydrogen pressure of 1 to 10 atm. for about 0.5 to 10 hours. In the reaction, an acid such as hydrochloric acid may optionally added to the reaction system.

In case of the above method (ii), the reducing agent includes a mixture of iron, zinc, tin or stannous chloride and a mineral acid (e.g. hydrochloric acid, sulfuric acid, etc.), or a mixture of iron, ferrous sulfate, zinc or tin and an alkali metal hydroxide (e.g. sodium hydroxide, etc.), a sulfide (e.g. ammonium sulfide, etc.), aqueous ammonia, or an ammonium salt (e.g. ammonium chloride, etc.). The inert solvent includes, for example water, acetic acid, methanol, ethanol, dioxane, and the like. The reducing reaction conditions are determined depending on the kinds of the reducing agent, but in case of using a reducing agent comprising stannous chloride and hydrochloric acid, for example, it is preferably carried out at a temperature of about  $0^{\circ}\text{C}$  to room temperature for about 0.5 to 10 hours. The reducing agent is usually used in an

amount of at least one mole, preferably 1 to 5 moles, to 1 mole of the starting compound.

[Reaction Scheme-20]



wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $R^{17}$ ,  $R^{18}$ ,  $2$ ,  $2'$ ,  $2''$  and  $W$  are as

defined above, and  $R^{36}$  is a lower alkyl,  $R^{37}$  is a lower alkanoyl, and  $R^{35}$  is hydrogen atom, a lower alkyl or a lower alkanoyl.

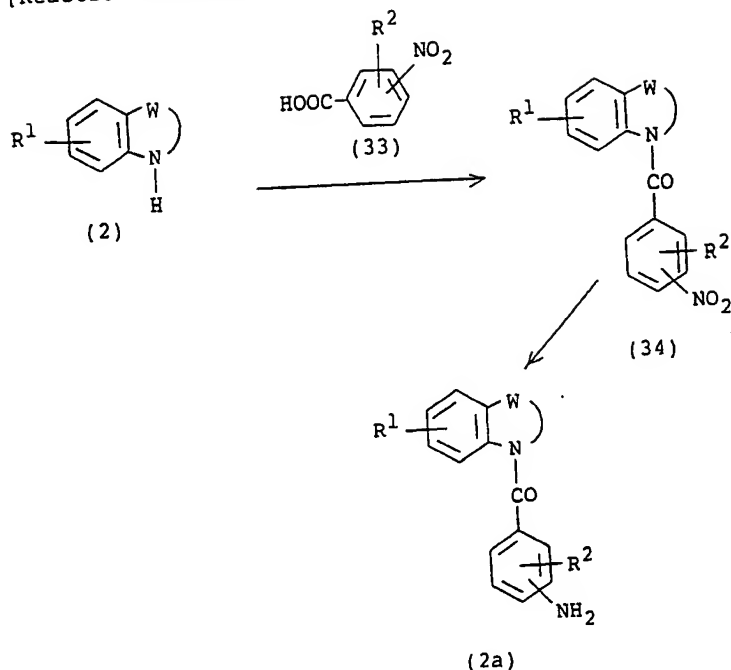
The reaction of the compound (1S) and the compound (31) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1S) and the compound (32) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1. Besides, the compound (1U) can also be obtained by reacting the compound (1S) with a compound of the formula:  $(R^{37})_2O$  ( $R^{37}$  is as defined above). The reaction is carried out under the same conditions as in the above reaction of the compound (1p) and a compound of the formula:  $(R^{7b})_2O$ .

The compound (1) wherein  $R^8$  is a phenyl-lower alkoxy carbonyl can be converted into the compound (1) wherein  $R^8$  is hydrogen atom in the same manner as in the reaction of converting the compound (1I) into the compound (1J) in the above Reaction Scheme-16.

Other derivatives of the starting compound (2) can be prepared, for example, by the process shown in the following reaction scheme.

[Reaction Scheme-21]



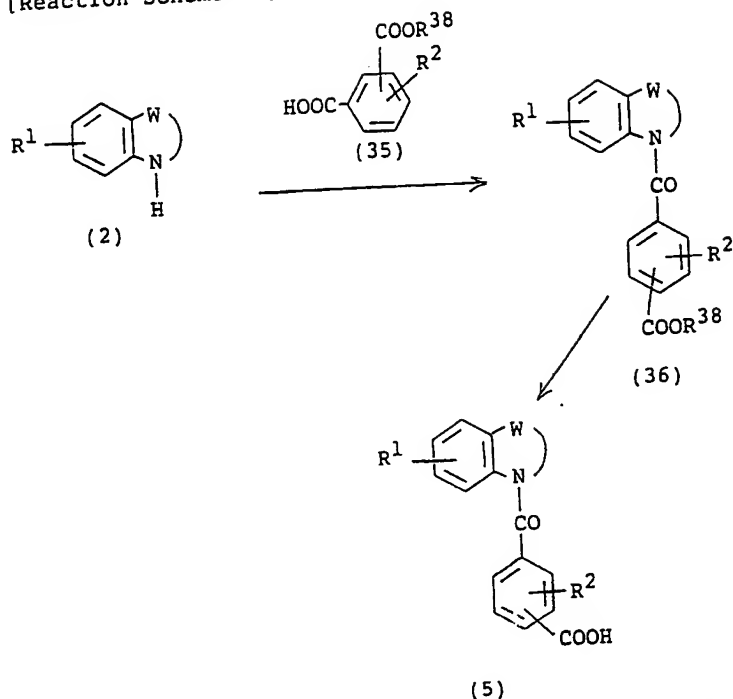
wherein  $R^1$ ,  $R^2$ , and  $W$  are as defined above.

The reaction of the compound (2) and the compound (33) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of converting the compound (34) into the compound (2a) can be carried out under the same conditions as in the reducing reaction in the above Reaction Scheme-19.

The starting compound (5) can be prepared, for example, by the process of the following reaction scheme.

[Reaction Scheme-22]

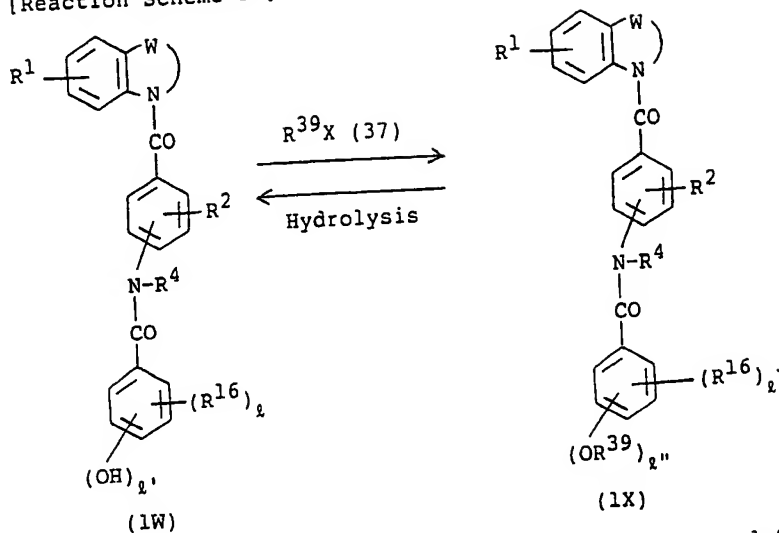


wherein R<sup>1</sup>, R<sup>2</sup>, and W are as defined above, and R<sup>38</sup> is a lower alkyl.

The reaction of the compound (2) and the compound (35) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of converting the compound (36) into the compound (5) can be carried out under the same conditions as in the hydrolysis reaction in the above Reaction Scheme-7.

[Reaction Scheme-23]

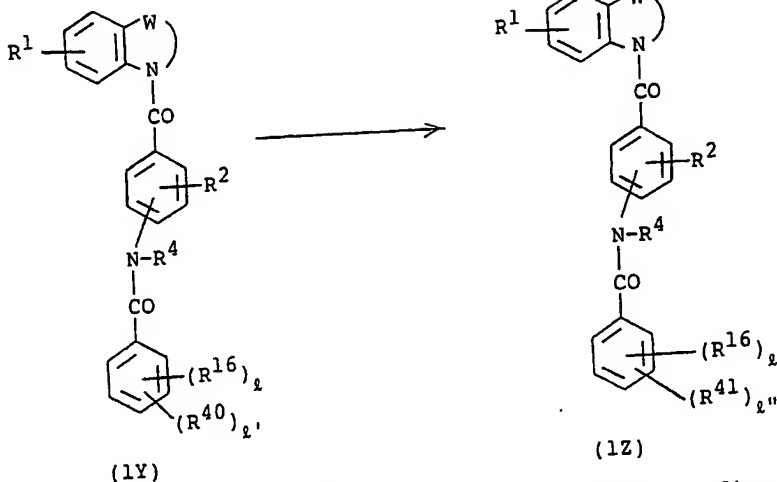


wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $\ell$ ,  $\ell'$ ,  $\ell''$ ,  $X$ , and  $W$  are as defined above, and  $R^{39}$  is a lower alkanoyl.

The reaction of the compound (1W) and the compound (37) can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

The hydrolysis reaction of the compound (1X) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the above Reaction Scheme-7.

[Reaction Scheme-24]

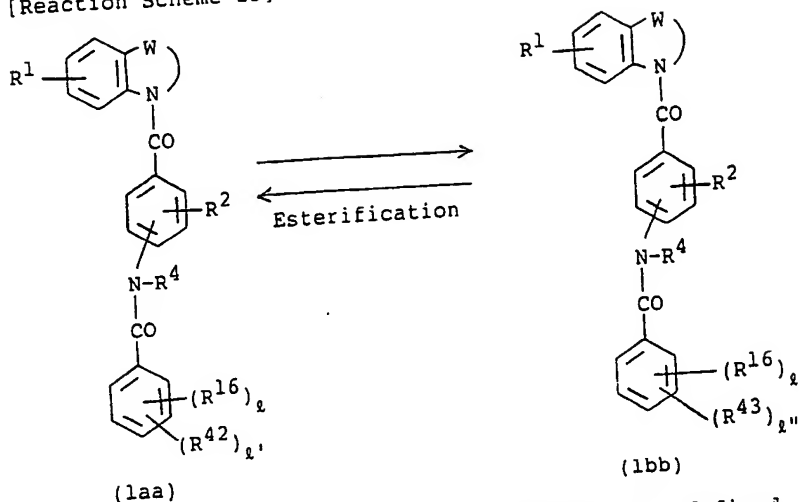


wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $z$ ,  $z'$ ,  $z''$ , and  $W$  are as defined above,  $R^{40}$  is a lower alkanoyl, and  $R^{41}$  is a hydroxy-substituted lower alkyl.

The reaction of converting the compound (1Y) into the compound (1Z) can be carried out under the same conditions as in the reaction of converting the compound (1A) into the compound (1B) in the above Reaction Scheme-15.



[Reaction Scheme-25]

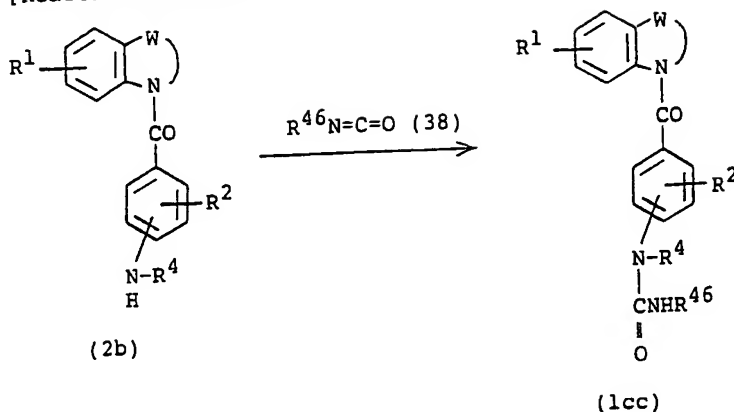


wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $R^{16}$ ,  $2$ ,  $2'$ ,  $2''$ , and  $W$  are as defined above,  $R^{42}$  is a lower alkoxy carbonyl and  $R^{43}$  is carboxyl.

The reaction of converting the compound (1aa) into the compound (1bb) can be carried out under the same conditions as in the hydrolysis of the compound (1j) in the above Reaction Scheme-7.

The esterification reaction of the compound (1bb) can be carried out under the same conditions as in the esterification of the compound (1w) in the above Reaction Scheme-13.

[Reaction Scheme-26]

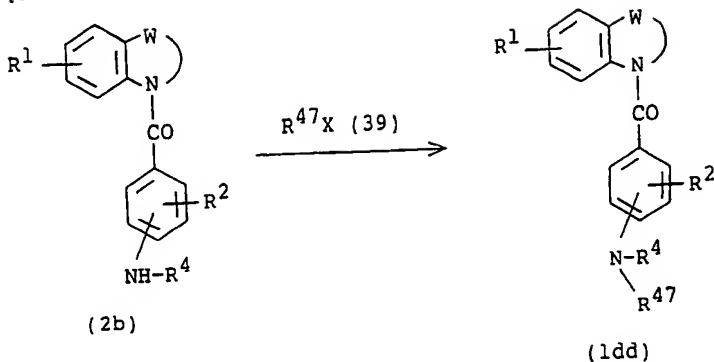


wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, and W are as defined above, and R<sup>46</sup> is a phenyl having optionally a lower alkyl substituent.

The reaction of the compound (2b) and the compound (38) is usually carried out in an appropriate solvent or without solvent in the presence or absence, preferably in the absence, of a basic compound. The solvent and basic compound are the same as those used in the reaction of the carboxylic acid halide and the amine (2) in the above Reaction Scheme-1.

The compound (38) is usually used in an amount of about 1 to 5 moles, preferably about 1 to 3 moles, to 1 mole of the compound (2b). The reaction is usually carried out at a temperature of from about 0°C to about 200°C, preferably from room temperature to about 150°C, for about 5 minutes to about 30 hours. In the reaction, a boron compound (e.g. boron trifluoride etherate, etc.) may be added to the reaction system.

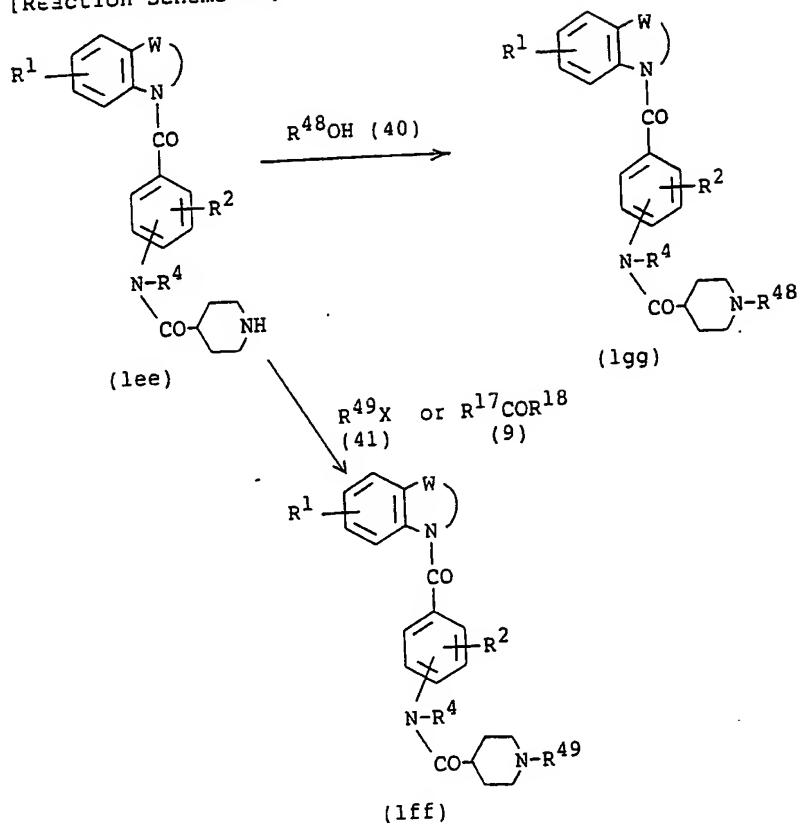
[Reaction Scheme-27]



wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, W, and X are as defined above, and R<sup>47</sup> is a phenylsulfonyl which has optionally a substituent selected from a halogen atom and a lower alkyl on the phenyl ring, or quinolylsulfonyl.

The reaction of the compound (2b) and the compound (39) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

[Reaction Scheme-28]



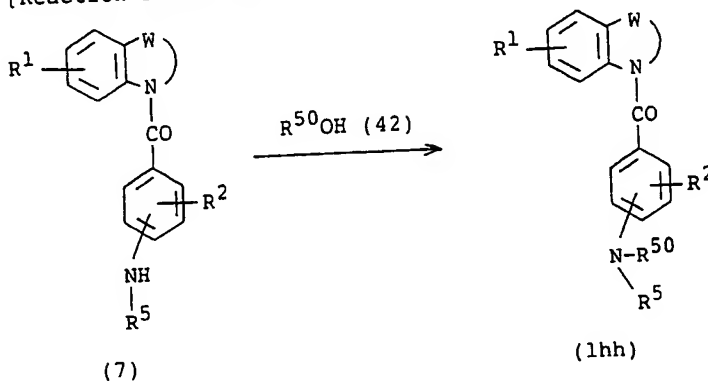
wherein  $R^1$ ,  $R^2$ ,  $R^4$ ,  $W$ ,  $R^{17}$ ,  $R^{18}$ , and  $X$  are as defined above,  $R^{48}$  is a phenyl-lower alkoxy carbonyl, a lower alkanoyl, an amino-lower alkanoyl having optionally a lower alkyl substituent, and  $R^{49}$  is a lower alkyl or a carbamoyl-lower alkyl.

The reaction of the compound (lee) and the compound (40) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the

above Reaction Scheme-1.

The reaction of the compound (lee) and the compound (41) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4, provided that in the reaction product (lff) produced by the reaction of the compound (lee) and the compound (9), the group  $R^{49}$  is a lower alkyl.

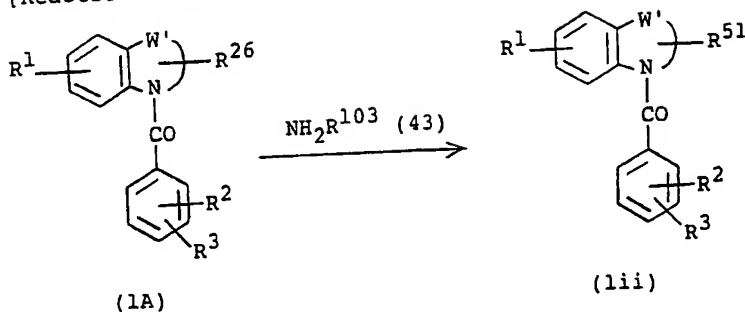
[Reaction Scheme-29]



wherein  $R^1$ ,  $R^2$ ,  $R^5$ , and  $W$  are as defined above, and  $R^{50}$  is a benzoyl having optionally a halogen substituent on the phenyl ring.

The reaction of the compound (7) and the compound (42) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

[Reaction Scheme-30]

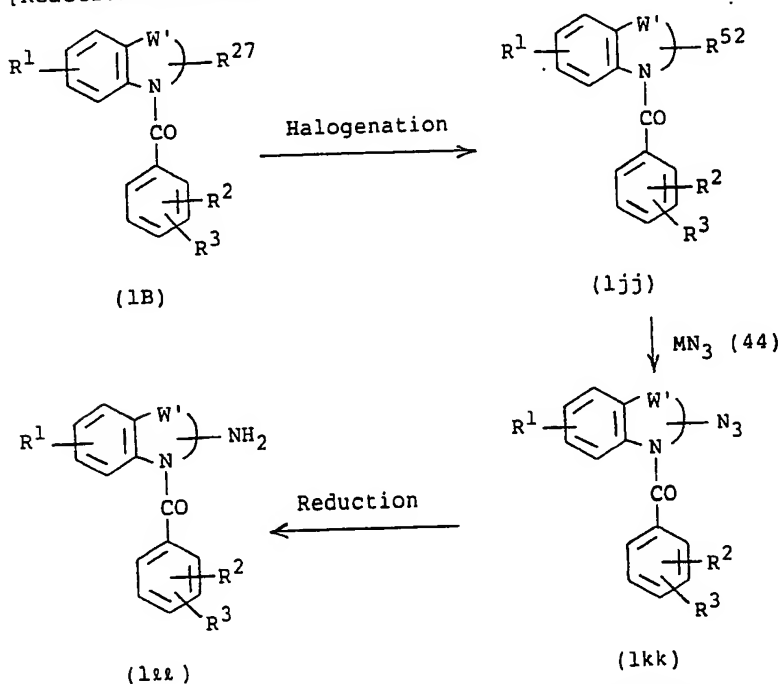


wherein  $\text{R}^1$ ,  $\text{W}'$ ,  $\text{R}^{26}$ ,  $\text{R}^2$ , and  $\text{R}^3$  are as defined above,  $\text{R}^{103}$  is hydroxy or sulfoxy, and  $\text{R}^{51}$  is hydroxyimino or sulfoxyimino.

The reaction of the compound (1A) and the compound (43) is usually carried out in an appropriate inert solvent in the presence or absence of a basic compound. The basic compound includes, for example, inorganic basic compounds such as sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, etc., and organic basic compounds such as piperidine, pyridine, triethylamine, 1,5-diazabicyclo[4.3.0]nonene-5 (DBN), 1,8-diazabicyclo[5.4.0]undecene-7 (DBU), 1,4-diazabicyclo[2.2.2]octane (DABCO), etc. The inert solvent includes, for example, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, ethylene glycol monomethyl ether, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), halogenated hydrocarbons (e.g. dichloromethane, dichloroethane, chloroform, carbon tetrachloride, etc.), pyridine,

dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc., or a mixture of these solvents. The compound (43) is usually used at least in equivalent amount, preferably 1 to 5 moles, to 1 mole of the compound (1A). The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from about 50°C to 150°C, for about 1 to 10 hours.

[Reaction Scheme-31]



wherein  $R^1$ ,  $W'$ ,  $R^{27}$ ,  $R^2$ ,  $M$ , and  $R^3$  are as defined above, and  $R^{52}$  is a halogen atom.

The halogenation of the compound (1B) is usually carried out in an appropriate solvent or without solvent by

reacting the compound (1B) with a halogenating agent.

The halogenating agent includes mineral acids (e.g. hydrochloric acid, hydrobromic acid, etc.), N,N-diethyl-1,2,2-trichlorovinylamide, phosphorus pentachloride, phosphorus pentabromide, phosphorus oxychloride, thionyl chloride, methanesulfonyl chloride, or a combination of a phenyl-lower alkyl halide (e.g. p-toluenesulfonyl chloride, etc.) and a basic compound. The basic compound includes the same compounds as used in the reaction of the compound (1A) and the compound (43) in the above Reaction Scheme-30. The solvent includes, for example, ethers (e.g. dioxane, tetrahydrofuran, etc.), halogenated hydrocarbons (e.g. chloroform, methylene chloride, carbon tetrachloride, etc.), and the like. The amount of the halogenating agent may vary depending on the kinds of the halogenating agents, and in case of a combination of a phenyl-lower alkyl halide (e.g. p-toluenesulfonyl chloride, etc.) and a basic compound, it is used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the compound (1B), and in case of other halogenating agents, it is used at least in an equimolar amount, usually in a largely excess amount, to the compound (1B). The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 80°C, for about 1 to 80 hours.

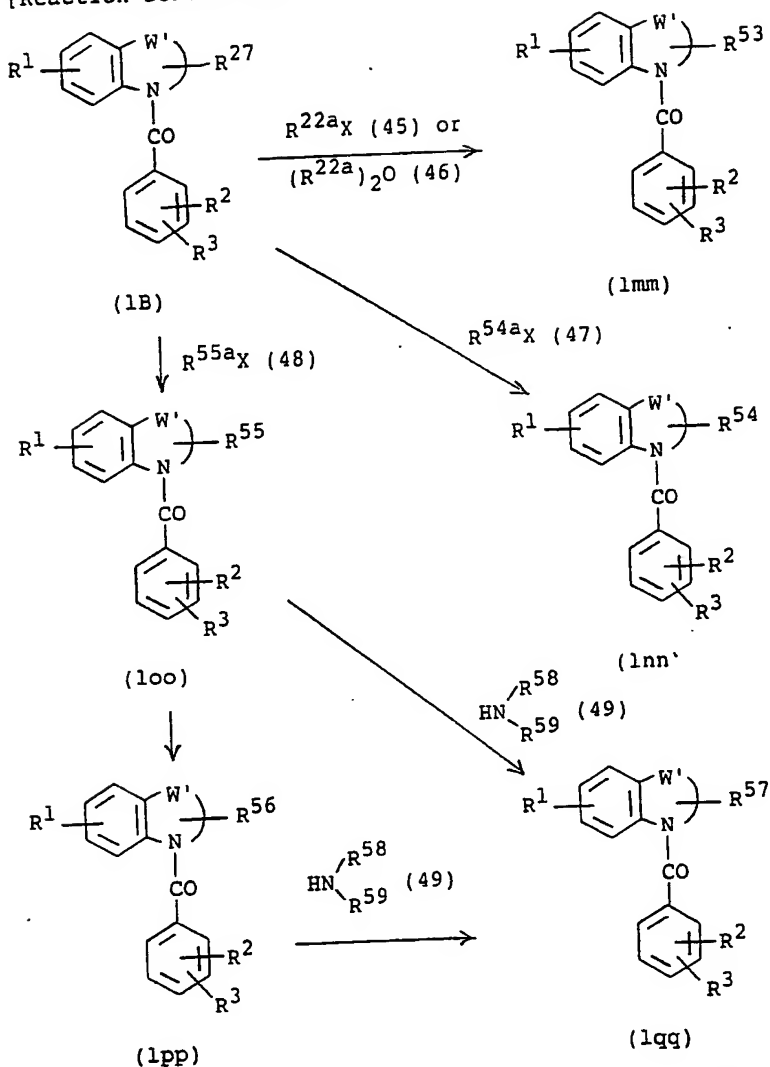
The reaction of the compound (1jj) and the compound (44) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the



above Reaction Scheme-4.

The reducing reaction of the compound (1kk) can be carried out under the same conditions as in the reducing reaction using a reducing catalyst for converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

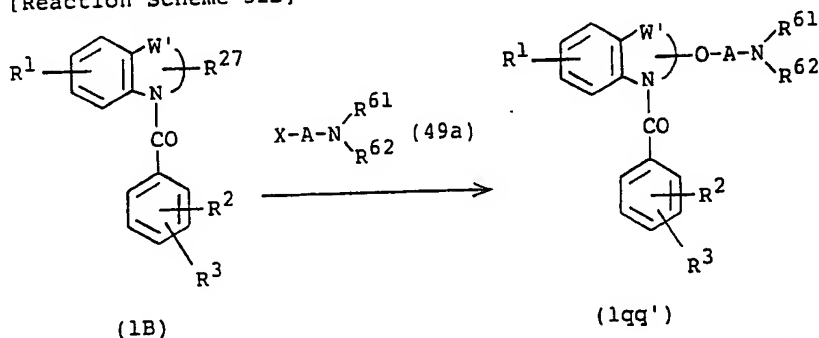
## [Reaction Scheme-32A]



wherein  $R^1$ ,  $W'$ ,  $R^2$ ,  $R^3$ ,  $R^{27}$ ,  $X$ , and  $A$  are as defined above,  $R^{53}$  is a lower alkanoyloxy having optionally a halogen substituent,  $R^{54}$  is a lower alkoxy, an amino-lower alkanoyloxy having optionally a lower alkyl substituent, or a group of the formula:

$-O-A-CON \begin{matrix} R^{82} \\ R^{83} \end{matrix}$  (A,  $R^{82}$  and  $R^{83}$  are as defined above),  $R^{55}$  is a lower alkoxycarbonyl-substituted lower alkoxy,  $R^{56}$  is a carboxy-substituted lower alkoxy,  $R^{57}$  is an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent,  $R^{54a}$  is a lower alkyl, an amino-lower alkanoyl having optionally a lower alkyl substituent, or a group of the formula:  $-A-CON \begin{matrix} R^{82} \\ R^{83} \end{matrix}$  (A,  $R^{82}$  and  $R^{83}$  are as defined above),  $R^{55a}$  is a lower alkoxy-carbonyl-substituted lower alkyl,  $R^{58}$  and  $R^{59}$  are the same or different and are each hydrogen atom or a lower alkyl, and  $R^{22a}$  is a lower alkanoyl having optionally a halogen substituent.

[Reaction Scheme-32B]



wherein  $R^1$ ,  $W'$ ,  $R^2$ ,  $R^3$ ,  $X$ ,  $R^{27}$ , and  $A$  are as defined above, and  $R^{61}$  and  $R^{62}$  are the same or different and are each hydrogen atom, a lower alkyl or a lower alkanoyl.

The reaction of the compound (1B) and the compound (45) or the compound (46) in the Reaction Scheme-32A can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

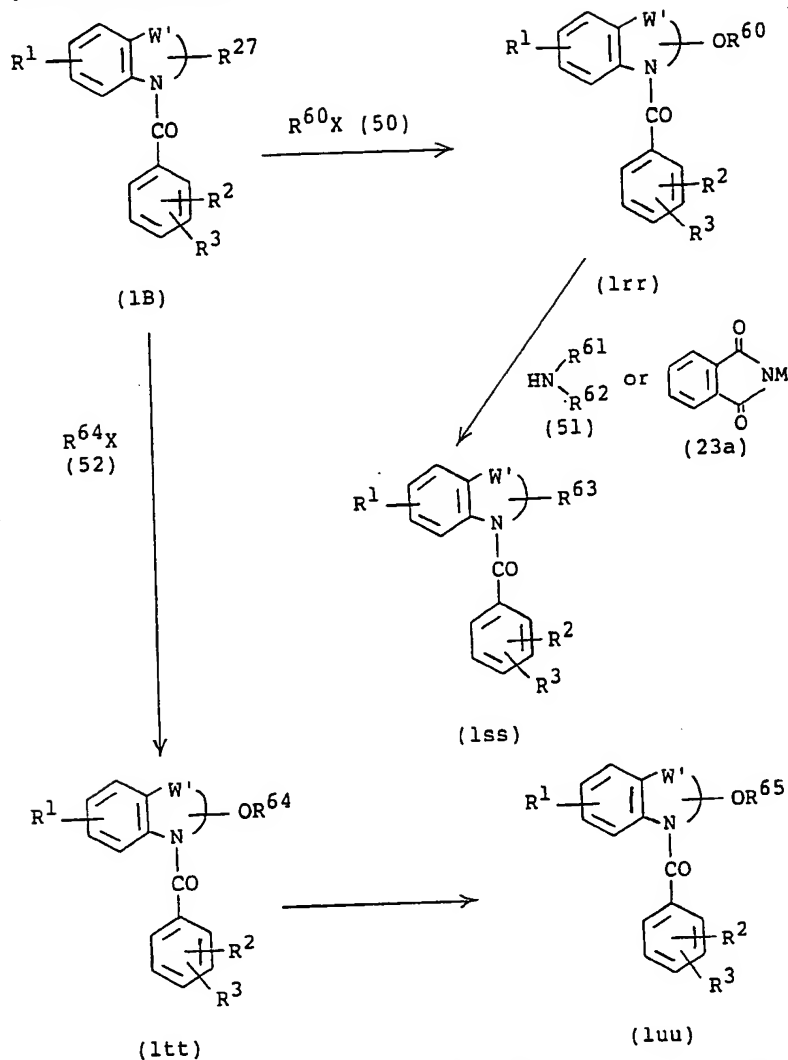
The reaction of the compound (1B) and the compound (47) and the reaction of the compound (1B) and the compound (48) can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

The reaction of converting the compound (100) into the compound (1pp) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1j) in the above Reaction Scheme-7.

The reaction of the compound (100) and the compound (49) and the reaction of the compound (1pp) and the compound (49) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1B) and the compound (49a) in the Reaction Scheme-32B can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

## [Reaction Scheme-33]



wherein  $R^1$ ,  $W'$ ,  $R^2$ ,  $R^3$ ,  $R^{27}$ ,  $R^{61}$ ,  $R^{62}$ ,  $M$ , and  $X$  are as defined above,  $R^{60}$  is a halogen-substituted lower alkyl,  $R^{64}$  is a phthalimido-substituted lower alkyl,  $R^{63}$  is an amino-

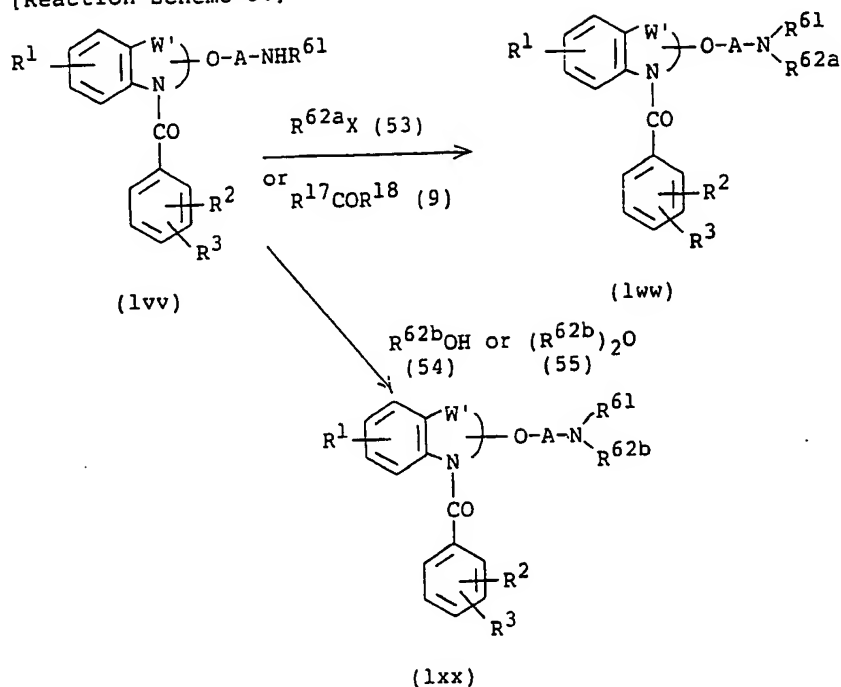
lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl, or a phthalimido-substituted lower alkoxy, and  $R^{65}$  is an amino-substituted lower alkyl.

The reaction of the compound (1B) and the compound (50) and the reaction of the compound (1B) and the compound (52) can be carried out under the same conditions as in the reaction of the compound (1n) and the compound (18) in the above Reaction Scheme-9.

The reaction of the compound (1rr) and the compound (51) or the compound (23a) can be carried out under the same conditions as in the reaction of the compound (1g) and the compound (14) in the above Reaction Scheme-6.

The reaction of converting the compound (1tt) into the compound (1uu) can be carried out under the same conditions as in the reaction of converting the compound (1j) into the compound (1k) in the above Reaction Scheme-7.

[Reaction Scheme-34]



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^{61}$ ,  $\text{W}'$ ,  $\text{A}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$ , and  $\text{X}$  are as defined above,  $\text{R}^{62a}$  is a lower alkyl, and  $\text{R}^{62b}$  is a lower alkanoyl.

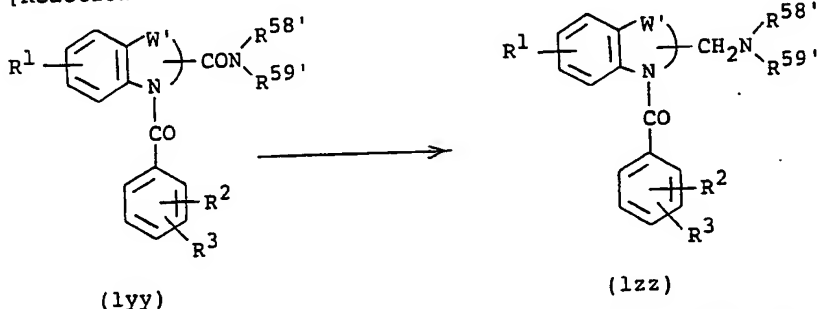
The reaction of the compound (1vv) and the compound (53) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1vv) and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the

above Reaction Scheme-1.

The reaction of the compound (lvv) and the compound (55) can be carried out under the same conditions as in the reaction of the compound (lp) and the compound of the formula:  $(R^{7b})_2O$  in the above Reaction Scheme-10.

[Reaction Scheme-35]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $W'$  are as defined above,  $R^{58'}$  and  $R^{59'}$  are the same or different and are each hydrogen atom, a lower alkyl, or a lower alkanoyl.

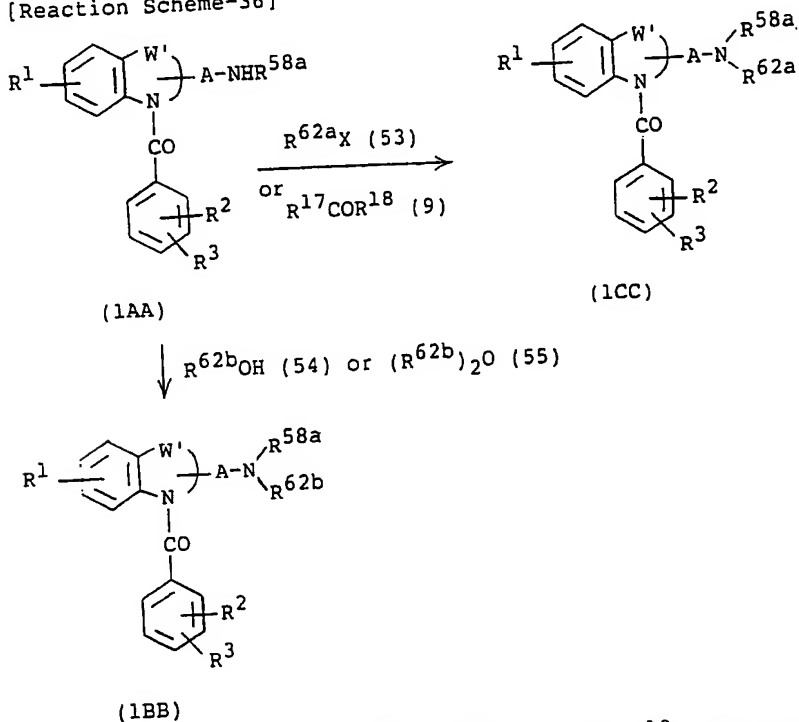
The reaction of converting the compound (lyy) into the compound (lzz) is usually carried out by reducing the compound (lyy).

The reducing reaction is preferably carried out by using a hydrogenating reducing agent. The hydrogenating reducing agent includes, for example, lithium aluminum hydride, sodium boro hydride, diborane, etc. The reducing agent is usually used in an amount of at least one mole, preferably 1 to 15 moles, to 1 mole of the starting compound. The reducing reaction is usually carried out in an appropriate solvent, such as water, lower alcohols (e.g.



methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diisopropyl ether, diglyme, etc.), or a mixture of these solvents, at a temperature of about  $-60^{\circ}\text{C}$  to about  $150^{\circ}\text{C}$ , preferably about  $-30^{\circ}\text{C}$  to  $100^{\circ}\text{C}$ , for about 10 minutes to about 5 hours. When lithium aluminum hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as diethyl ether, tetrahydrofuran, diglyme, etc.

[Reaction Scheme-36]



wherein  $\text{R}^1$ ,  $\text{W}'$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^{62a}$ ,  $\text{R}^{62b}$ ,  $\text{X}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$ , and  $\text{A}$  are as defined above,  $\text{R}^{58a}$  is hydrogen atom, a lower alkyl or a lower alkanoyl.

The reaction of the compound (1AA) and the compound (53) or the compound (9) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) or the compound (9) in the above Reaction Scheme-4.

The reaction of the compound (1AA) and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1AA) and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula:  $(R^{7b})_2O$  in the above Reaction Scheme-10.

The compound (1BB) wherein  $R^{62b}$  is formyl can also be prepared by reacting the compound (1AA) with a formate of the formula:  $HCOOR^{82}$  under the same conditions as in the reaction of the compound (1K) and the compound of the formula:  $HCOOR^{82}$  as described hereinbefore.

The compounds of the formula (1) wherein W is sulfur atom or sulfinyl, or  $R^{82}$  and  $R^{83}$  bind together with the nitrogen atom to which they bond to form thiomorpholino or 1-oxo-thiomorpholino can be converted into the corresponding compounds of the formula (1) wherein W is sulfinyl or sulfonyl, or  $R^{82}$  and  $R^{83}$  bind together with the nitrogen atom to which they bond to form 1-oxo-thiomorpholino or 1,1-dioxo-thiomorpholino, respectively, by oxidation thereof.

The oxidation reaction is carried out in an

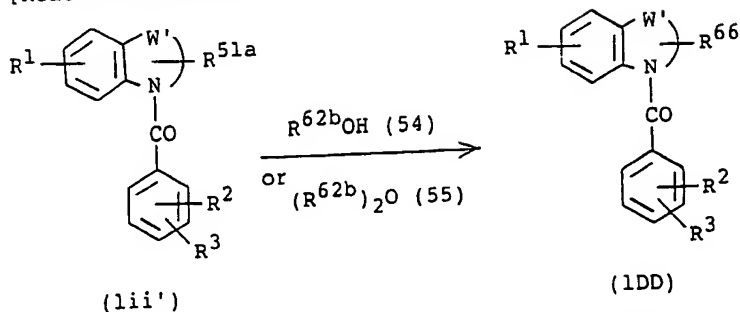
appropriate solvent in the presence of an oxidizing agent. The solvent includes, for example, water, organic acids (e.g. formic acid, acetic acid, trifluoroacetic acid, etc.), alcohols (e.g. methanol, ethanol, etc.), halogenated hydrocarbons (e.g. chloroform, dichloromethane, etc.), or a mixture of these solvents. The oxidizing agent includes, for example, peracids (e.g. performic acid, peracetic acid, trifluoro-peracetic acid, perbenzoic acid, m-chloro-perbenzoic acid, o-carboxy-perbenzoic acid, etc.), hydrogen peroxide, sodium metaperiodate, dichromic acid, dichromates (e.g. sodium dichromate, potassium dichromate, etc.), permanganic acid, permanganates (e.g. potassium permanganate, sodium permanganate, etc.), lead salts (e.g. lead tetraacetate, etc.), and the like. The oxidizing agent is usually used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the starting compound. Besides, in cases of the oxidation of converting the sulfur atom into sulfonyl group, the oxidizing agent is usually used at least 2 moles, preferably 2 to 4 moles, to 1 mole of the starting compound. The above reaction is usually carried out at a temperature of about  $-10^{\circ}\text{C}$  to about  $40^{\circ}\text{C}$ , preferably from about  $-10^{\circ}\text{C}$  to room temperature, for about 1 to 100 hours.

The compound (1) wherein  $\text{R}^{16}$  or  $\text{R}^2$  is a lower alkoxy can be converted into the correspond compound (1) wherein  $\text{R}^{16}$  or  $\text{R}^2$  is hydroxy by heating the compound in a mixture of an acid (e.g. hydrobromic acid, hydrochloric acid, etc.) and a solvent (e.g. water, methanol, ethanol,

isopropyl alcohol, etc.) at 30 to 150°C, preferably at 50 to 120°C.

Besides, the compound (1) wherein  $R^{16}$  or  $R^2$  is hydroxy can also be prepared by hydrolysis of the above compound (1) wherein  $R^{16}$  or  $R^2$  is a lower alkoxy. The hydrolysis can be carried out in an appropriate solvent in the presence of an acid. The solvent includes, for example, water, lower alcohols (e.g. methanol, ethanol, isopropyl alcohol, etc.), ethers (e.g. dioxane, tetrahydrofuran, etc.), halogenated hydrocarbons (e.g. dichloromethane, chloroform, carbon tetrachloride, etc.), polar solvents (e.g. acetonitrile, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, hydrobromic acid, etc.), Lewis acids (e.g. boron trifluoride, aluminum chloride, boron tribromide, etc.), iodides (e.g. sodium iodide, potassium iodide, etc.), or a mixture of the above Lewis acid and iodide. The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for about 0.5 to 30 hours.

## [Reaction Scheme-37]

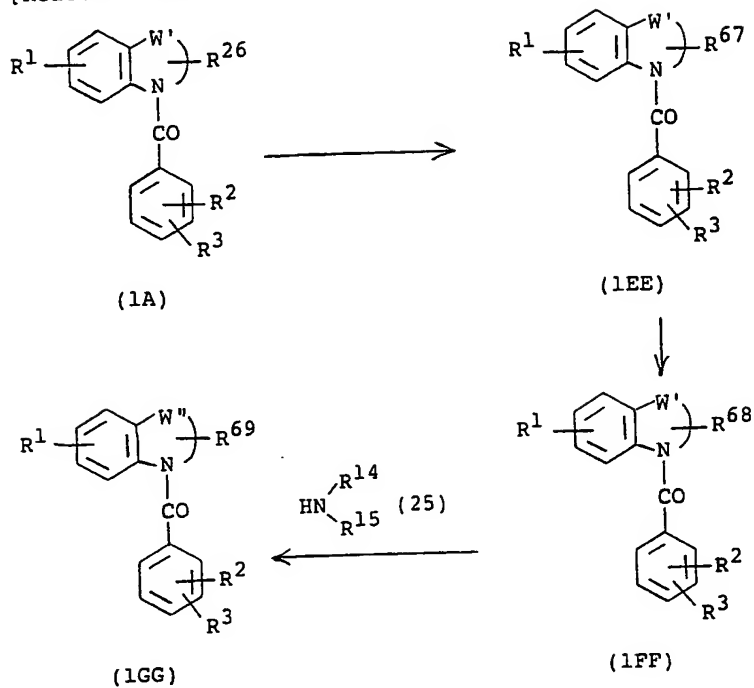


wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>62b</sup>, and W' are as defined above, R<sup>51a</sup> is hydroxyimino, and R<sup>66</sup> is a lower alkanoyloxyimino.

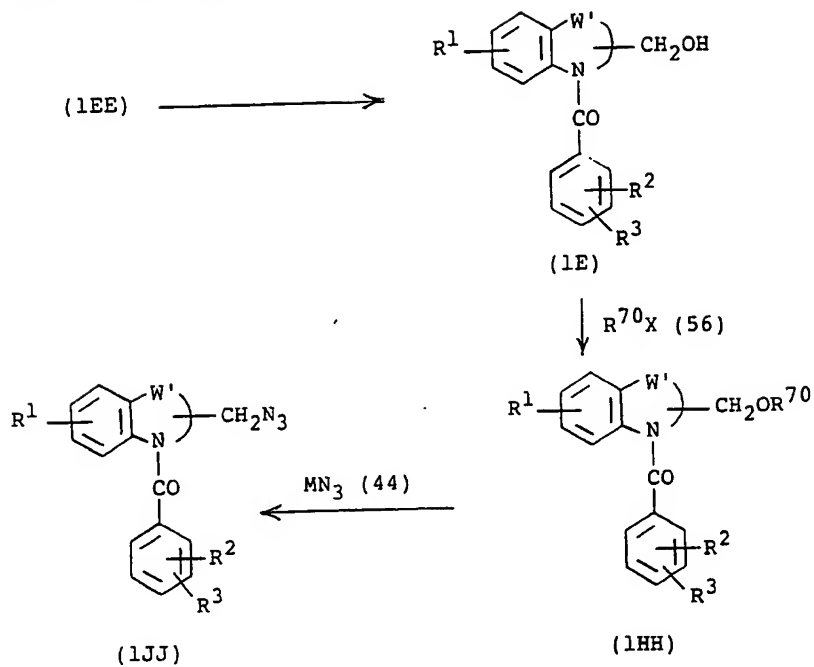
The reaction of the compound (lii') and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (lii') and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula: (R<sup>7b</sup>)<sub>2</sub>O in the above Reaction Scheme-10.

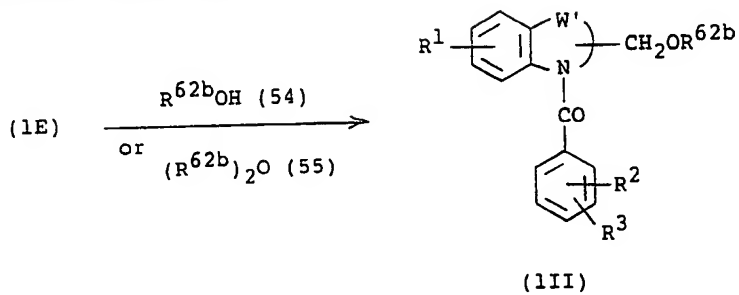
## [Reaction Scheme-38A]



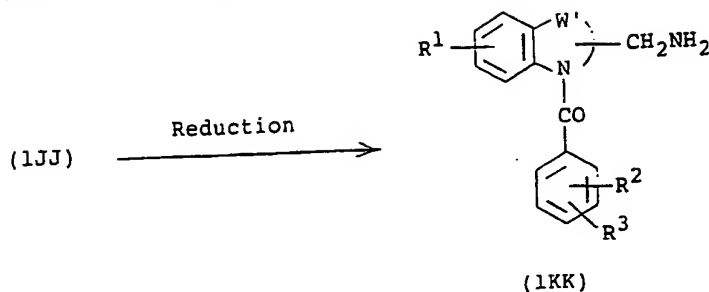
[Reaction Scheme-38B]



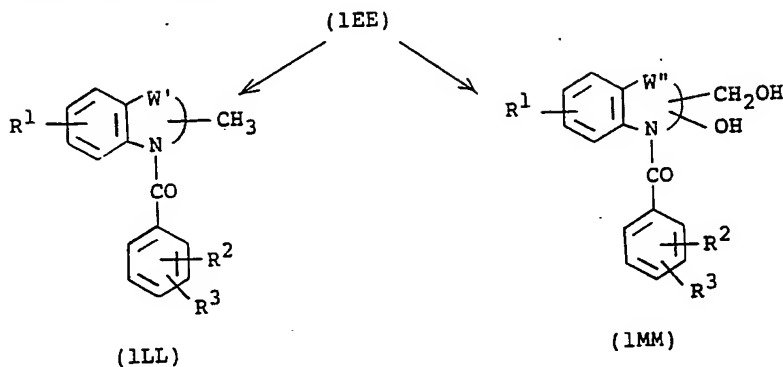
[Reaction Scheme-38C]



## [Reaction Scheme-38D]



## [Reaction Scheme-38E]



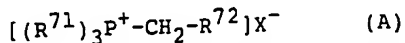
wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $R^{26}$ ,  $R^{14}$ ,  $R^{15}$ ,  $R^{62b}$ ,  $X$  and  $M$  are as defined above,  $R^{67}$  is methyldiene,  $R^{68}$  is a group of the

formula:  $\begin{array}{c} \diagup \\ \diagdown \end{array} O$ , and  $R^{69}$  is a group of the formula:  $\begin{array}{c} CH_2OH \\ \diagdown \\ NR^{14}R^{15} \end{array}$   
 ( $R^{14}$  and  $R^{15}$  are as defined above), or  $\begin{array}{c} CH_2R^{7D} \\ \diagdown \\ OH \end{array}$  ( $R^{7D}$  is an

amino having optionally a substituent selected from a lower alkyl and a lower alkanoyl,  $R^{70}$  is a lower alkylsulfonyl, and  $W''$  is the same as the above  $W$ , provided that the number of the substituent in the groups  $-(CH_2)_p-$  and  $-CH=CH-(CH_2)_q-$  is 0 or 1.



The reaction of converting the compound (1A) into the compound (1EE) is carried out in an appropriate solvent in the presence of a Wittig reagent and a basic compound. The Wittig reagent includes, for example, a phosphoric compound of the formula:



wherein  $R^{71}$  is phenyl,  $R^{72}$  is hydrogen atom or a lower alkyl, and X is a halogen atom. The basic compound includes inorganic bases (e.g. metallic sodium, metallic potassium, sodium hydride, sodium amide, sodium hydroxide, potassium hydroxide, sodium carbonate, potassium carbonate, sodium hydrogen carbonate, etc.), metal alcoholates (e.g. sodium methyllate, sodium ethyllate, potassium t-butoxide, etc.), alkyl or aryl lithiums or lithium amides (e.g. methyl lithium, n-butyl lithium, phenyl lithium, lithium diisopropylamide, etc.), organic bases (e.g. pyridine, piperidine, quinoline, triethylamine, N,N-dimethylaniline, etc.). The solvent includes any solvent which does not affect on the reaction, for example, ethers (e.g. diethyl ether, dioxane, tetrahydrofuran, monoglyme, diglyme, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), aliphatic hydrocarbons (e.g. n-hexane, heptane, cyclohexane, etc.), amines (e.g. pyridine, N,N-dimethylaniline, etc.), aprotic polar solvents (e.g. N,N-dimethylformamide, dimethylsulfoxide, hexamethylphosphoric triamide, etc.), alcohols (e.g. methanol, ethanol, isopropanol, etc.), and the like. The reaction is usually carried out at a temperature of about  $-80^\circ\text{C}$  to about  $150^\circ\text{C}$ , preferably about  $-80^\circ\text{C}$  to about  $120^\circ\text{C}$ ,

for about 0.5 to 15 hours.

The reaction of converting the compound (1EE) into the compound (1LL) can be carried out under the same conditions as in the catalytically hydrogenation reaction for converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

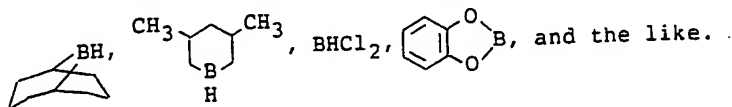
The reaction of converting the compound (1EE) into the compound (1FF) is carried out under the same conditions as in the reaction of converting the compound (1) wherein W is sulfur atom or sulfinyl into the corresponding compound (1) wherein W is sulfinyl or sulfonyl respectively as described herebefore.

The reaction of the compound (1FF) and the compound (25) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reaction of converting the compound (1EE) into the compound (1E) can be carried out by firstly subjecting it to hydroboration reaction and then to oxidation.

The hydroboration reaction is carried out in a solvent such as ethers (e.g. diethyl ether, tetrahydrofuran, dioxane, etc.) in the presence of a hydroborating agent at a temperature of from about 0°C to about 50°C, preferably about 0°C to room temperature, for about 1 to 10 hours. The hydroborating agent includes boron hydride compounds, for example,  $\text{BH}_3$ .tetrahydrofuran,  $\text{BH}_3 \cdot \text{S}(\text{CH}_3)_2$ ,  $\text{BH}_2\text{Cl}$ ,

$(\text{CH}_3)_2\text{CHC}(\text{CH}_3)_2\text{BH}_2$ ,  $(\text{CH}_3)_2\text{CHCH}(\text{CH}_3)\text{BH}$ ,  $(\text{C}_6\text{H}_{11})_2\text{BH}$ ,  $(\text{C}_6\text{H}_5)_2\text{BH}$ ,



The subsequent oxidation is carried out in water in the presence of an oxidizing agent. The oxidizing agent includes, for example, alkaline hydrogen peroxides (e.g. hydrogen peroxide - sodium hydroxide, etc.), and air oxidation is also used. The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for 0.5 to 7 hours.

The hydroborating agent and the oxidizing agent are each used in an amount of at least 1 mole, preferably 1 to 2 mole, to 1 mole of the compound (1EE).

The reaction of the compound (1E) and the compound (54) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The reaction of the compound (1E) and the compound (55) can be carried out under the same conditions as in the reaction of the compound (1p) and the compound of the formula:  $(R^{7b})_2O$  in the above Reaction Scheme-10.

The reaction of the compound (1E) and the compound (56) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

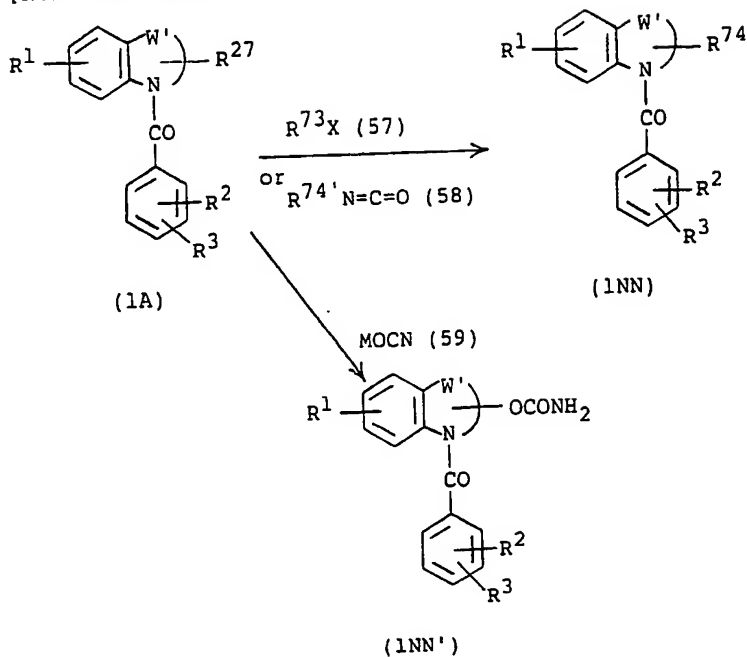
The reaction of the compound (1HH) and the compound (44) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reducing reaction of the compound (1JJ) can be carried out under the same conditions as in the catalytic hydrogenation reaction for converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

The reaction of converting the compound (1EE) into the compound (1MM) can be carried out by reacting with an oxidizing agent in an appropriate solvent in the presence of a co-oxidizing agent.

The solvent used for the reaction with an oxidizing agent includes, for example, pyridine, ethers (e.g. dioxane, tetrahydrofuran, diethyl ether, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), halogenated hydrocarbons (e.g. dichloromethane, dichloroethane, chloroform, carbon tetrachloride, etc.), esters (e.g. ethyl acetate, etc.), water, alcohols (e.g. methanol, ethanol, isopropanol, t-butanole, etc.), or a mixture of these solvents. The co-oxidizing agent includes, for example, organic amine N-oxides (e.g. pyridine N-oxide, N-ethyldiisopropylamine N-oxide, N-methylmorpholine N-oxide, trimethylamine N-oxide, triethylamine N-oxide, etc.). The oxidizing agent includes, for example, osmium tetroxide, and the like. The oxidizing agent is usually used in an amount of at least 1 mole, preferably 1 to 5 moles, to 1 mole of the starting compound. The reaction is usually carried out at a temperature of from -20°C to 150°C, preferably from room temperature to 100°C, for about 1 to 10 hours.

[Reaction Scheme-39]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^{27}$ ,  $W'$ ,  $M$ , and  $X$  are as defined above,  $R^{73}$  is an aminocarbonyl having optionally a lower alkyl substituent,  $R^{74}$  is an aminocarbonyloxy having optionally a lower alkyl substituent,  $R^{74}'$  is a lower alkyl.

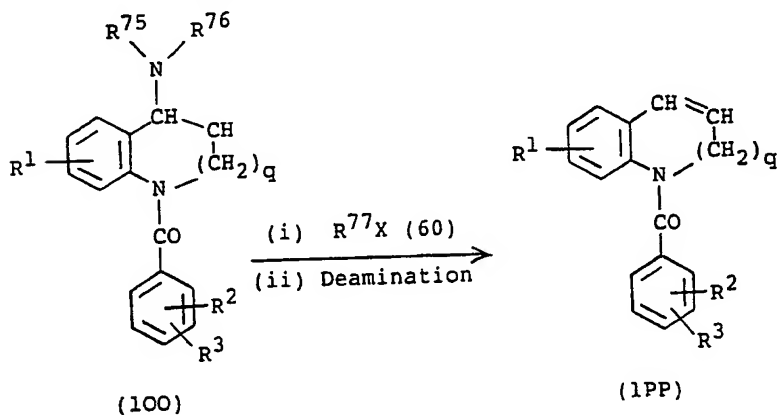
The reaction of the compound (1A) and the compound (57) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reaction of the compound (1A) and the compound (59) is carried out in an appropriate solvent in the presence of an acid. The solvent includes the same solvent

as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. The acid includes, for example, mineral acids (e.g. hydrochloride acid, sulfuric acid, etc.), sulfonic acids (e.g. methanesulfonic acid, p-toluenesulfonic acid, etc.), alkanolic acids (e.g. trifluoroacetic acid, etc.), and the like. The compound (59) is used in an amount of at least 1 mole, preferably 1 to 5 moles, to 1 mole of the compound (1A). The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for about 1 to 7 hours.


The reaction of the compound (1A) and the compound (58) can be carried out under the same conditions as in the reaction of the compound (2b) and the compound (38) in the above Reaction Scheme-26.

[Reaction Scheme-40]



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{X}$ , and  $q$  are as defined above, and  $\text{R}^{75}$ ,  $\text{R}^{76}$  and  $\text{R}^{77}$  are each a lower alkyl, and the carbon atom in the formula:  $-(\text{CH}_2)_q-$  may be substituted by oxygen atom,

sulfur atom, sulfinyl, sulfonyl, or a group of the formula:

$$\begin{array}{c} R^{13} \\ | \\ -N- \end{array}$$
 ( $R^{13}$  is as defined above), and further the group:  $-(CH_2)_q-$  may optionally have 1 to 3 substituents selected from a lower alkyl having optionally a hydroxy substituent, a lower alkoxy-carbonyl, carboxyl, hydroxy, oxo, a lower alkanoyloxy having optionally a halogen substituent, an amino-lower alkyl having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a lower alkanoyloxy-substituted lower alkyl, a lower alkylsulfonyloxy-lower alkyl, an azido-lower alkyl, a group of the formula: , an aminocarbonyloxy having optionally a lower alkyl substituent, a lower alkoxy, a lower alkoxy-carbonyl-substituted lower alkoxy, a carboxy-substituted lower alkoxy, an aminocarbonyl-lower alkoxy having optionally a lower alkyl substituent, an amino-lower alkoxy having optionally a substituent selected from a lower alkyl and a lower alkanoyl, a phthalimido-substituted lower alkoxy, hydroxyimino, a lower alkanoyloxyimino, a lower alkylidene, a halogen atom, azido, sulfoxyimino, a group of the formula:  $R^{81}-N-CH_2COO-$  ( $R^{81}$  is

hydrogen atom or a lower alkyl), hydrazino, pyrrolyl, an amino-lower alkanoyloxy having optionally a lower alkyl substituent,

a group of the formula:  $-O-A-CO-N \begin{array}{l} R^{82} \\ R^{83} \end{array}$  (A is as defined above,

and  $R^{82}$  and  $R^{83}$  are the same or different and are each hydrogen atom, a lower alkyl, a carbamoyl-substituted lower alkyl, a hydroxy-substituted lower alkyl, or a pyridyl-lower alkyl, or  $R^{82}$  and  $R^{83}$  may bind together with nitrogen atom to which they

bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen, oxygen or sulfur atom wherein the heterocyclic group has optionally a substituent selected from oxo, a lower alkyl, a lower alkanoyl, and carbamoyl), and a group of the formula:  $-(CO)_n-N \begin{matrix} R^{14} \\ R^{15} \end{matrix}$  (n is as defined above, and  $R^{14}$  and  $R^{15}$  are the same or different and are each hydrogen atom, a lower alkyl, a lower alkenyl, a lower alkanoyl, a cycloalkyl, an oxiranyl-substituted lower alkyl, a lower alkyl having 1 to 2 substituents selected from a lower alkoxy, hydroxy and an amino having optionally a lower alkyl substituent, a phenyl-lower alkyl, a pyridyl-lower alkyl, a lower alkylsulfonyl, benzoyl, a lower alkoxycarbonyl, anilino-carbonyl, an aminocarbonyl having optionally a lower alkyl substituent, a cyano-substituted lower alkyl, a lower alkoxy-carbonyl-substituted lower alkyl, a carbamoyl-substituted lower alkyl, a carboxy-substituted lower alkyl, a tetrahydropyranyl-oxy-substituted lower alkyl, a lower alkanoyloxy-substituted lower alkyl, a piperidinyl having optionally a phenyl-lower alkyl substituent on the piperidinyl ring, a halogen-substituted lower alkanoyl, an imidazolyl-substituted lower alkanoyl, an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl, an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, or a phenyl-lower alkoxycarbonyl, or  $R^{14}$  and  $R^{15}$  may bind together in the nitrogen atom to which they bond to form a 5- or 6-membered saturated heterocyclic group with or without being intervened with nitrogen or oxygen atom, which

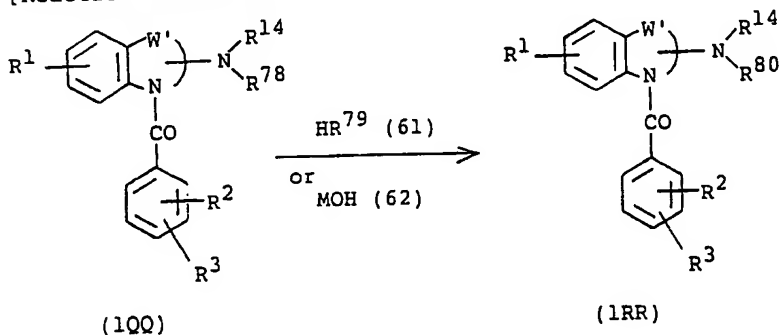


heterocyclic group may optionally have a substituent selected from a lower alkyl, a phenyl-lower alkyl and a lower alkanoyl.

The reaction of the compound (100) and the compound (60) is carried out in an appropriate solvent in an autoclave. The solvent includes any solvent as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 1 to 7 hours.

The subsequent deamination reaction is carried out in an appropriate solvent in the presence of a basic compound. The solvent includes the same solvent as used in the above reaction of the compound (100) and the compound (60). The basic compound includes any basic compound as used in the reaction of converting the compound (1A) into the compound (1EE) in the above Reaction Scheme-38. The reaction is usually carried out at a temperature of from room temperature to about 150°C, preferably from room temperature to about 100°C, for about 1 to 10 hours.

[Reaction Scheme-41]



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^{14}$ ,  $\text{M}$ , and  $\text{W}'$  are as defined above,  $\text{R}^{78}$  is

an oxiranyl-substituted lower alkyl,  $R^{79}$  is a lower alkoxy, or an amino having optionally a lower alkyl substituent, and  $R^{80}$  is a lower alkyl having 2 substituents selected from hydroxy, a lower alkoxy, and an amino having optionally a lower alkyl substituent.

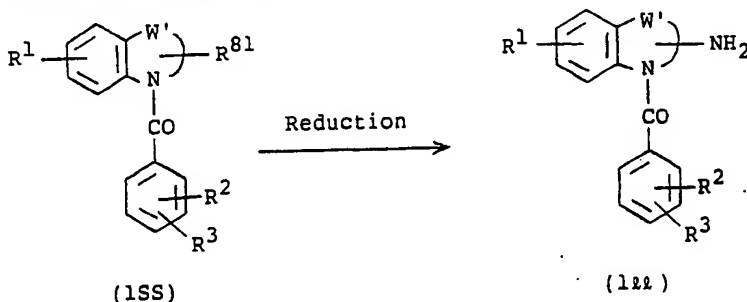
The reaction of the compound (1QQ) and the compound (61) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

The reaction of the compound (1QQ) and the compound (62) can be carried out by firstly reacting them in trifluoroacetic acid at a temperature of about  $0^{\circ}\text{C}$  to about  $100^{\circ}\text{C}$ , preferably about  $0^{\circ}\text{C}$  to about  $50^{\circ}\text{C}$ , for about 1 to 7 hours, followed by hydrolysis of the resultant.

The hydrolysis is carried out in an appropriate solvent or without solvent in the presence of an acid or a basic compound. The solvent includes, for example, water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ketones (e.g. acetone, methyl ethyl ketone, etc.), ethers (e.g. dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, etc.), fatty acids (e.g. acetic acid, formic acid, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, sulfuric acid, hydrobromic acid, etc.), organic acids (e.g. formic acid, acetic acid, aromatic sulfonic acid, etc.), and the like. The basic compound includes, for example, metal carbonates (e.g. sodium carbonate, potassium carbonate, etc.), metal hydroxides (e.g. sodium hydroxide, potassium hydroxide, calcium hydroxid ,

etc.). The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 0.5 to 25 hours.

[Reaction Scheme-42]



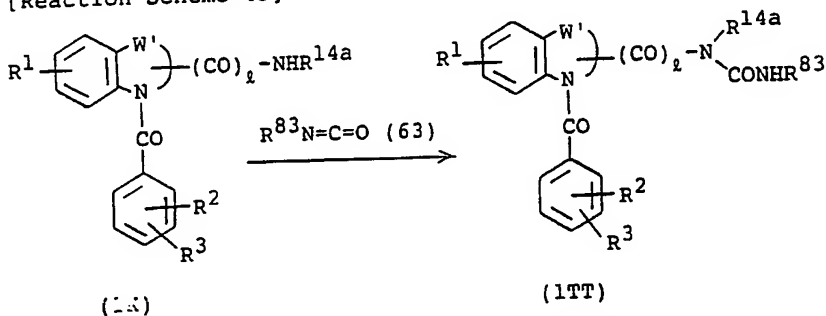
wherein R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, and W' are as defined above, and R<sup>81</sup> is hydroxyimino or a lower alkanoyloxyimino.

The reaction of converting the compound (1SS) into the compound (122) is carried out by catalytically hydrogenating the compound (1SS) in an appropriate solvent in the presence of a catalyst. The solvent includes, for example, water, acetic acid, alcohols (e.g. methanol, ethanol, isopropanol, etc.), hydrocarbons (e.g. hexane, cyclohexane, etc.), ethers (e.g. diethylene glycol dimethyl ether, dioxane, tetrahydrofuran, diethyl ether, etc.), esters (e.g. ethyl acetate, methyl acetate, etc.), aprotic polar solvents (e.g. dimethylformamide, etc.), or a mixture of these solvents. The catalyst includes, for example, palladium, palladium black, palladium-carbon, platinum, platinum oxide, copper chromate, Raney nickel, and the like. The catalyst is usually used in an amount of 0.02 to 1 part by weight to 1 part by weight of the compound (1SS). The reaction is usually carried out at a temperature of from

about  $-20^{\circ}\text{C}$  to about  $100^{\circ}\text{C}$ , preferably about  $0^{\circ}\text{C}$  to about  $70^{\circ}\text{C}$ , under a hydrogen atmospheric pressure of 1 to 10 atm. for about 0.5 to 20 hours.

Alternatively, the reducing reaction can also be carried out by using a hydrogenating reducing agent. The hydrogenating reducing agent includes, for example, lithium aluminum hydride, sodium boro hydride, diborane, etc. The reducing agent is usually used in an amount of at least one mole, preferably 1 to 10 moles, to 1 mole of the compound (1SS). The reaction is usually carried out in an appropriate solvent, such as water, lower alcohols (e.g. methanol, ethanol, isopropanol, etc.), ethers (e.g. tetrahydrofuran, diethyl ether, diglyme, etc.), acetic acid, and the like, at a temperature of about  $0^{\circ}\text{C}$  to about  $200^{\circ}\text{C}$ , preferably about  $0^{\circ}\text{C}$  to  $170^{\circ}\text{C}$ , for about 10 minutes to about 10 hours. When lithium aluminum hydride or diborane is used as the reducing agent, it is preferable to use an anhydrous solvent such as diethyl ether, tetrahydrofuran, diglyme, etc.

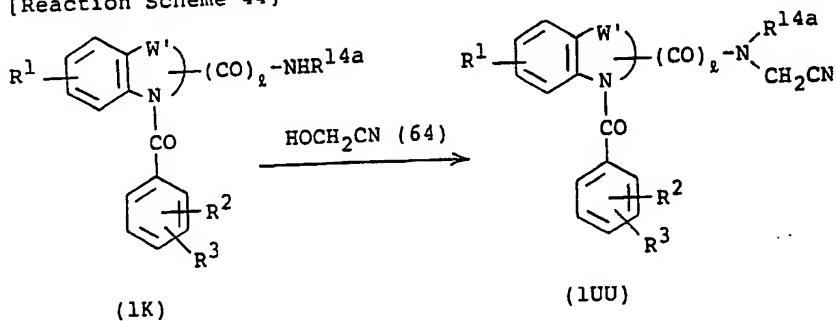
[Reaction Scheme-43]



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{W}'$ ,  $\text{R}^{14a}$  are as defined above, and  $\text{R}^{83}$  is phenyl or a lower alkyl.

The reaction of the compound (1K) and the compound (63) can be carried out under the same conditions as in the reaction of the compound (2b) and the compound (38) in the above Reaction Scheme-26.

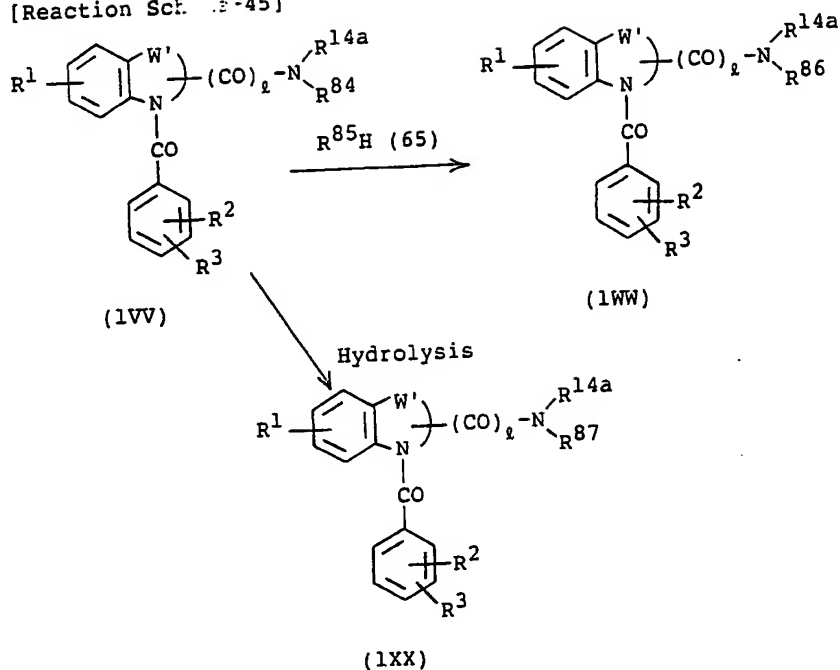
[Reaction Scheme-44]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $l$ ,  $R^{14a}$  are as defined above.

The reaction of the compound (1K) and the glyconitrile (64) can be carried out in an appropriate solvent. The solvent includes the same solvent as used in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4. The reaction is usually carried out at a temperature of from about  $0^\circ C$  to about  $150^\circ C$ , preferably about  $0^\circ C$  to about  $100^\circ C$ , for about 1 to 10 hours. The glyconitrile (64) is used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the compound (1K).

[Reaction Scheme-45]

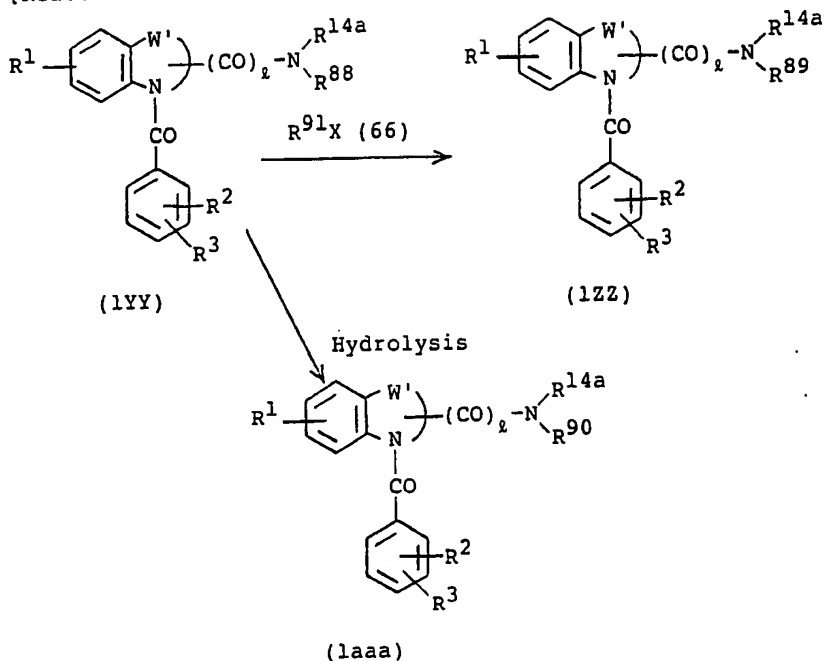


wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $\epsilon$ ,  $R^{14a}$  are as defined above,  $R^{84}$  is a lower alkoxy-carbonyl-substituted lower alkyl,  $R^{85}$  is an amino having optionally a lower alkyl substituent,  $R^{86}$  is an aminocarbonyl-lower alkyl having optionally a lower alkyl substituent, and  $R^{87}$  is a carboxy-substituted lower alkyl.

The reaction of the compound (1VV) and the compound (65) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

The hydrolysis reaction of the compound (1VV) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1QQ) and the compound (62) in the above Reaction Scheme-41.

[Reaction Scheme-46]

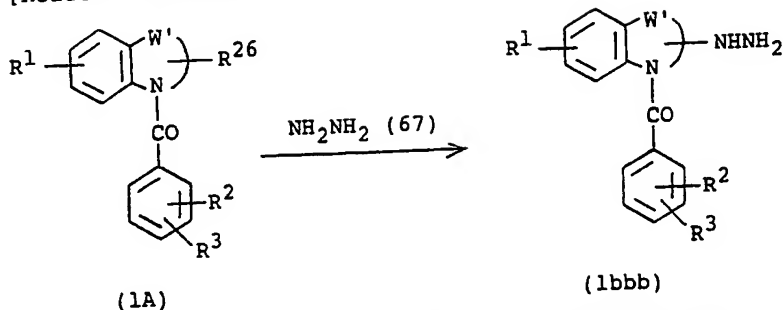


wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $x$ ,  $X$ , and  $R^{14a}$  are as defined above,  $R^{88}$  is a tetrahydropyranyloxy-substituted lower alkyl,  $R^{89}$  is a lower alkanoyloxy-substituted lower alkyl,  $R^{90}$  is a hydroxy-substituted lower alkyl, and  $R^{91}$  is a lower alkanoyl.

The reaction of the compound (1YY) and the compound (66) can be carried out in a solvent such as acetic acid at a temperature of about  $0^\circ\text{C}$  to about  $200^\circ\text{C}$ , preferably about  $0^\circ\text{C}$  to about  $150^\circ\text{C}$ , for about 0.5 to 15 hours.

The hydrolysis reaction of the compound (1YY) can be carried out under the same conditions as in the hydrolysis reaction of the compound (1QQ) and the compound (62) in the above Reaction Scheme-41, wherein a pyridinium salt (e.g. pyridinium p-toluenesulfonate, etc.) may be used as the acid.

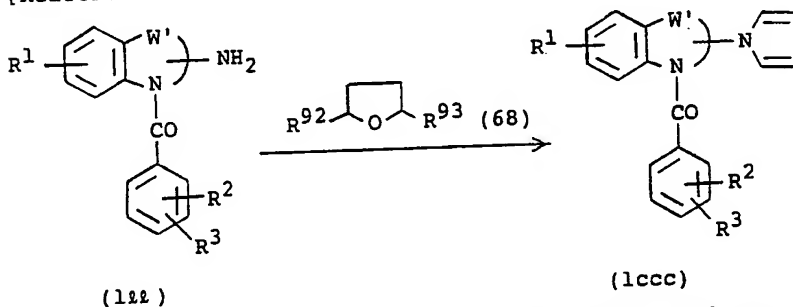
## [Reaction Scheme-47]



wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{W}'$ , and  $\text{R}^{26}$  are as defined above.

The reaction of converting the compound (1A) into the compound (1bbb) can be carried out under the same conditions as in the reaction of converting the compound (1A) into the compound (1C) in the above Reaction Scheme-15.

## [Reaction Scheme-48]



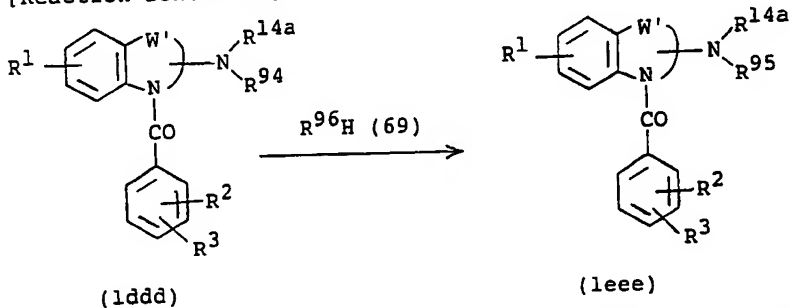
wherein  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$  and  $\text{W}'$  are as defined above,  $\text{R}^{92}$  and  $\text{R}^{93}$  are each a lower alkoxy.

The reaction of the compound (1ll) and the compound (68) is carried out in an appropriate solvent in the presence of an acid. The solvent includes, for example, water, alcohols (e.g. methanol, ethanol, isopropanol, etc.), ketones (e.g. acetone, methyl ethyl ketone, etc.), ethers (e.g. dioxane, tetrahydrofuran, ethylene glycol dimethyl ether, etc.), fatty



acids (e.g. acetic acid, formic acid, etc.), or a mixture of these solvents. The acid includes, for example, mineral acids (e.g. hydrochloric acid, sulfuric acid, hydrobromic acid, etc.), organic acids (e.g. formic acid, acetic acid, aromatic sulfonic acids, etc.). The reaction is usually carried out at a temperature of from room temperature to about 200°C, preferably from room temperature to about 150°C, for about 0.5 to 5 hours. The compound (68) is usually used in an amount of at least 1 mole, preferably 1 to 2 moles, to 1 mole of the compound (111).

[Reaction Scheme-49]

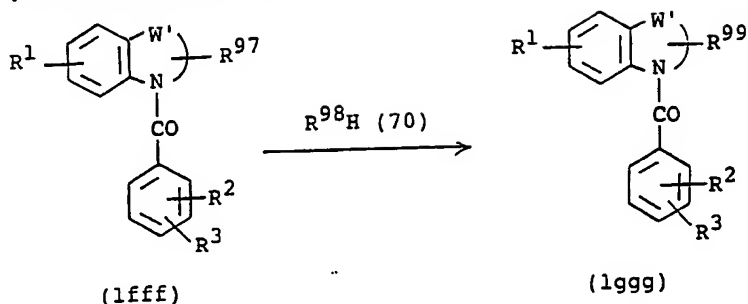


wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ , and  $R^{14a}$  are as defined above,  $R^{94}$  is a halogen-substituted lower alkanoyl,  $R^{95}$  is an imidazolyl-substituted lower alkanoyl or an amino-lower alkanoyl having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl, and  $R^{96}$  is imidazolyl, or an amino having optionally a substituent selected from a lower alkyl and a lower alkoxycarbonyl.

The reaction of the compound (1ddd) and the compound (69) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above

## Reaction Scheme-4.

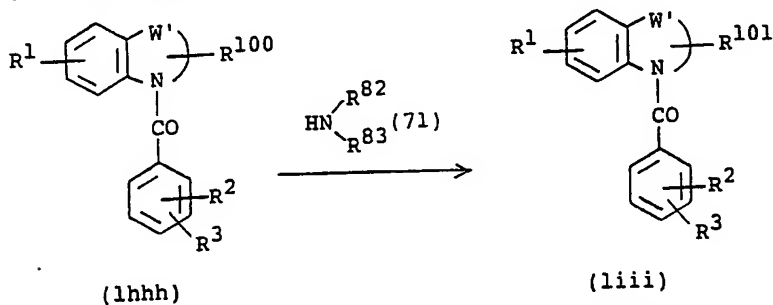
[Reaction Scheme-50]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ , and  $W'$  are as defined above,  $R^{97}$  is a lower alkanoyloxy having a halogen substituent,  $R^{98}$  is an amino having optionally a lower alkyl substituent, and  $R^{99}$  is an amino-lower alkanoyloxy having optionally a lower alkyl substituent.

The reaction of the compound (1fff) and the compound (70) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

[Reaction Scheme-51]

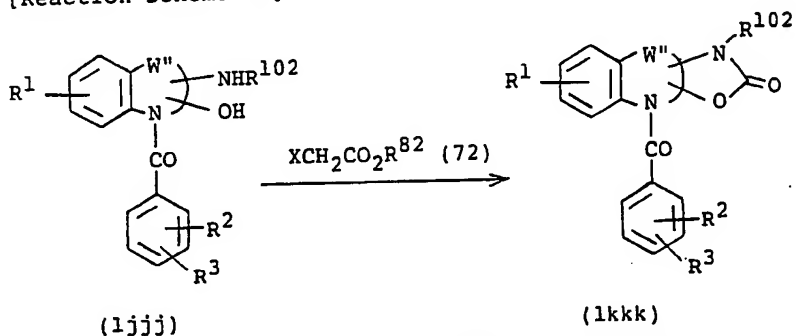


wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $R^{82}$ , and  $R^{83}$  are as defined above,  $R^{100}$  is a carboxy-substituted lower alkoxy, and  $R^{101}$  is a

group of the formula:  $-O-A-CON\begin{matrix} R^{82} \\ R^{83} \end{matrix}$  ( $A$ ,  $R^{82}$  and  $R^{83}$  are as defined above).

The reaction of the compound (1hhh) and the compound (71) can be carried out under the same conditions as in the reaction of the compound (2) and the compound (3) in the above Reaction Scheme-1.

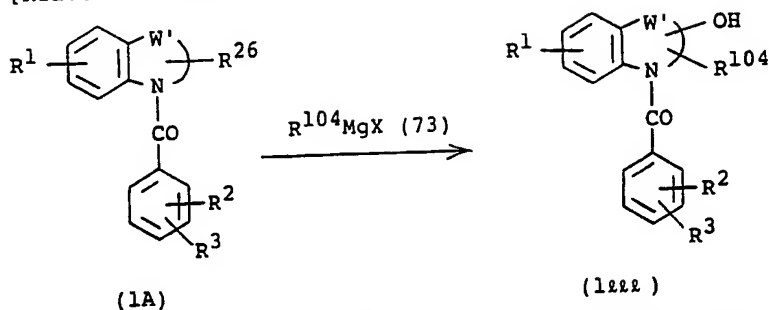
[Reaction Scheme-52]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W''$ ,  $X$ , and  $R^{82}$  are as defined above, and  $R^{102}$  is hydrogen atom or a lower alkyl, provided that in the compound (1jjj), the groups of the formulae:  $-NH-R^{102}$  and  $-OH$  are substituted at the positions adjacent each other.

The reaction of the compound (1jjj) and the compound (72) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

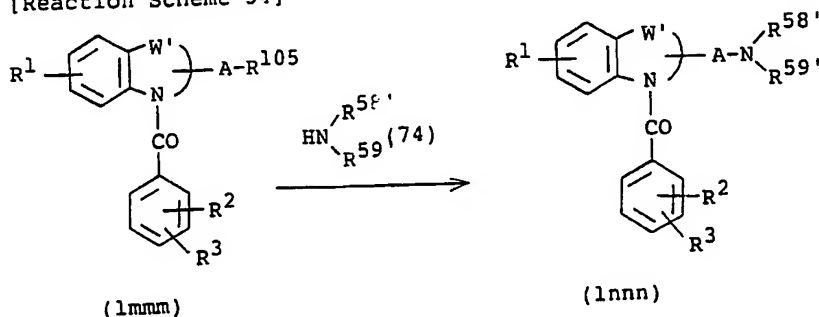
## [Reaction Scheme-53]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $R^{26}$  and  $X$  are as defined above, and  $R^{104}$  is a lower alkyl.

The reaction of the compound (1A) and the compound (73) can be carried out in an appropriate solvent. The solvent includes, for example, ethers (diethyl ether, dioxane, tetrahydrofuran, etc.), aromatic hydrocarbons (e.g. benzene, toluene, xylene, etc.), saturated hydrocarbons (e.g. pentane, hexane, heptane, cyclohexane, etc.), or a mixture of these solvents. The reaction is usually carried out at a temperature of from about  $-70^\circ C$  to about  $50^\circ C$ , preferably from about  $-30^\circ C$  to room temperature, for about 1 to 6 hours. The compound (73) is used in an amount of at least 1 mole, preferably 1 to 5 moles, to 1 mole of the compound (1A).

## [Reaction Scheme-54]



wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $W'$ ,  $R^{58'}$ ,  $R^{59'}$ , and A are as defined above, and  $R^{105}$  is a lower alkylsulfonyloxy.

The reaction of the compound (1mm) and the compound (74) can be carried out under the same conditions as in the reaction of the compound (7) and the compound (8) in the above Reaction Scheme-4.

Among the active compounds (1) of this invention, the compounds having an acidic group can easily be converted into salts by treating with a pharmaceutically acceptable basic compound. The basic compound includes, for example, metal hydroxides such as sodium hydroxide, potassium hydroxide, lithium hydroxide, calcium hydroxide, etc., alkali metal carbonates or hydrogen carbonates such as sodium carbonate, sodium hydrogen carbonate, etc., alkali metal alcoholates such as sodium methylate, potassium ethylate, etc. Besides, among the active compounds (1) of this invention, the compounds having a basic group can easily be converted into acid addition salts thereof by treating with a pharmaceutically acceptable acid. The acid includes, for example, inorganic acids such as sulfuric acid, nitric acid, hydrochloric acid, hydrobromic acid, etc., and organic acids such as acetic acid, p-toluene-sulfonic acid, ethanesulfonic acid, oxalic acid, maleic acid, fumaric acid, citric acid, succinic acid, benzoic acid, etc. These salts are useful as an active ingredient as like as the compounds (1) in the free form.

In addition, the compounds (1) of this invention include stereoisomers and optical isomers, and these isomers are also useful as the active ingredient in this invention.

The compounds of this invention thus obtained can easily be isolated and purified by conventional isolation methods. The isolation methods are, for example, distillation method, recrystallization method, column chromatography, ion exchange chromatography, gel chromatography, affinity chromatography, preparative thin layer chromatography, extraction with a solvent, and the like.

The compounds and their salts of this invention are useful as a vasopressin antagonist and are used in the form of a conventional pharmaceutical preparation. The preparation is prepared by using conventional dilutents or carriers such as fillers, thickening agents, binders, wetting agents, disintegrators, surfactants, lubricants, and the like. The pharmaceutical preparations may be selected from various forms in accordance with the desired utilities, and the representative forms are tablets, pills, powders, solutions, suspensions, emulsions, granules, capsules, suppositories, injections (solutions, suspensions, etc.), and the like. In order to form in tablets, there are used carriers such as vehicles (e.g. lactose, white sugar, sodium chloride, glucose, urea, starches, calcium carbonate, kaolin, crystalline cellulose, silicic acid, etc.), binders (e.g. water, ethanol, propanol, simple syrup, glucose solution, starch solution, gelatin solution, carboxymethyl cellulose, sodium alginate, methyl cellulose, potassium phosphate, polyvinylpyrrolidone, etc.), disintegrators (e.g. dry starch, sodium arginate, agar powder, laminaran powder, sodium hydrogen carbonate, calcium carbonate, polyoxyethylene sorbitan fatty acid esters, sodium laurylsulfate, stearic

monoglyceride, starches, lactose, etc.), disintegration inhibitors (e.g. white sugar, stearin, cacao butter, hydrogenated oils, etc.), absorption promoters (e.g. quaternary ammonium base, sodium laurylsulfate, etc.), wetting agents (e.g. glycerin, starches, etc.), adsorbents (e.g. starches, lactose, kaolin, bentonite, colloidal silicates, etc.), lubricants (e.g. purified talc, stearates, boric acid powder, polyethylene glycol, etc.), and the like. Moreover, the tablets may also be in the form of a conventional coated tablet, such as sugar-coated tablets, gelatin-coated tablets, enteric coated tablets, film coating tablets, or double or multiple layer tablets. In the preparation of pills, the carriers include vehicles (e.g. glucose, lactose, starches, cacao butter, hydrogenated vegetable oils, kaolin, talc, etc.), binders (e.g. gum arabic powder, tragacanth powder, gelatin, ethanol, etc.), disintegrators (e.g. laminaran, agar, etc.), and the like. In the preparation of suppositories, the carriers include, for example, polyethylene glycol, cacao butter, higher alcohols, higher alcohol esters, gelatin, semi-synthetic glycerides, and the like. Capsules can be prepared by charging a mixture of the compound of this invention with the above carriers into hard gelatin capsules or soft capsules in a usual manner. In the preparation of injections, the solutions, emulsions or suspensions are sterilized and are preferably made isotonic with the blood. In the preparation of these solutions, emulsions and suspensions, there are used conventional diluents, such as water, ethyl alcohol, macrogol

(propylene glycol), ethoxylated isostearyl alcohol, polyoxylated isostearyl alcohol, polyoxyethylene sorbitan fatty acid esters, and the like. In this case, the pharmaceutical preparations may also be incorporated with sodium chloride, glucose, or glycerin in an amount sufficient to make them isotonic, and may also be incorporated with conventional solubilizers, buffers, anesthetizing agents. Besides, the pharmaceutical preparations may optionally be incorporated with coloring agents, preservatives, perfumes, flavors, sweetening agents, and other medicaments, if required.

The amount of the active compound of this invention (active ingredient) to be incorporated into the anti-vasopressin preparations is not specified but may be selected from a broad range, but usually, it is preferably in the range of 1 to 70 % by weight, more preferably 5 to 50 % by weight.

The anti-vasopressin preparation of this invention may be administered in any method, and suitable method for administration may be determined in accordance with various forms of preparation, ages, sexes and other conditions of the patients, the degree of severity of diseases, and the like. For instance, tablets, pills, solutions, suspensions, emulsions, granules and capsules are administered orally. The injections are intravenously administered alone or together with a conventional auxiliary liquid (e.g. glucose, amino acid solutions), and further are optionally administered alone in intramuscular, intracutaneous, subcutaneous, or intraperitoneal route, if required. Suppositories are



administered in intrarectal route.

The dosage of the anti-vasopressin agent of this invention may be selected in accordance with the usage, ages, sexes and other conditions of the patients, the degree of severity of the diseases, and the like, but is usually in the range of about 0.6 to 50 mg of the active compound of this invention per 1 kg of body weight of the patient per day. The active compound is preferably contained in an amount of 10 to 1000 mg per the dosage unit.

#### Brief Description of Drawing

Fig. 1 to Fig. 4 show a chart of NMR ( $\text{CDCl}_3$ ) of the compounds in Examples 978 and 979.

#### Best Mode for Carrying Out the Invention

The present invention is illustrated by the following Preparations of anti-vasopressin agent, Reference Examples of processes for preparing the starting compounds to be used for preparing the active compounds, Examples of processes for preparing the active compounds, and Experiments of the activities of the active compounds of this invention.

#### Preparation 1

Film coated tablets are prepared from the following components.

<u>Components</u>	<u>Amount</u>
4-Methylamino-1-[4-(3,5-dichlorobenzoyl-amino)benzoyl]-1,2,3,4-tetrahydroquinoline	150 g

Avicel (tradename of microcrystalline cellulose, manufactured by Asahi Chemical Industry Co., Ltd., Japan)	40 g
Corn starch	30 g
Magnesium stearate	2 g
Hydroxypropyl methylcellulose	10 g
Polyethylene glycol-6000	3 g
Castor oil	40 g
Ethanol	40 g

The active component of this invention, Avicel, corn starch and magnesium stearate are mixed and kneaded and the mixture is tabletted using a conventional pounder (R 10 mm) for sugar coating. The tablets thus obtained are coated with a film coating agent consisting of hydroxypropyl methylcellulose, polyethylene glycol-6000, castor oil and ethanol to give film coated tablets.

#### Preparation 2

Tablets are prepared from the following components.

<u>Components</u>	<u>Amount</u>
1-[4-(N-Butylanilinoacetyl amino)benzoyl]- 2,3,4,5-tetrahydro-1H-benzazepine	150 g
Citric acid	1.0 g
Lactose	33.5 g
Dicalcium phosphate	70.0 g
Pullonic F-68	30.0 g
Sodium laurylsulfate	3.0 g
Polyvinylpyrrolidone	3.0 g
Polyethylene glycol (Carbowax 1500)	4.5 g

Polyethylene glycol (Carbowax 6000)	45.0 g
Corn starch	30.0 g
Dry sodium stearate	3.0 g
Dry magnesium stearate	3.0 g
Ethanol	q.s.

The active compound of this invention, citric acid, lactose, dicalcium phosphate, Pullonic F-68 and sodium lauryl stearate are mixed. The mixture is screened with No. 60 screen and is granulated with an alcohol solution containing polyvinylpyrrolidone, carbowax 1500 and 6000. If required, an alcohol is added thereto so that the powder mixture is made a paste-like mass. Corn starch is added to the mixture and the mixture is continuously mixed to form uniform particles. The resulting particles are passed through No. 10 screen and entered into a tray and then dried in an oven at 100°C for 12 to 14 hours. The dried particles are screened with No. 16 screen and thereto are added dry sodium laurylsulfate and dry magnesium stearate, and the mixture is tabletted to form the desired shape.

The core tablets thus prepared are vanished and dusted with talc in order to guard from wetting. Undercoating is applied to the core tablets. In order to administer the tablets orally, the core tablets are vanished several times. In order to give round shape and smooth surface to the tablets, further undercoating and coating with lubricant are applied thereto. The tablets are further coated with a coloring coating material until the desired

colored tablets are obtained. After drying, the coated tablets are polished to obtain the desired tablets having uniform gloss.

### Preparation 3

An injection preparation is prepared from the following components.

<u>Components</u>	<u>Amount</u>
4-Methyl-1-[4-(2,3-dimethylbenzoyl-amino)benzoyl]-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine	5 g
Polyethylene glycol (molecular weight: 4000)	0.3 g
Sodium chloride	0.9 g
Polyoxyethylene sorbitan monooleate	0.4 g
Sodium metabisulfite	0.1 g
Methyl-paraben	0.18 g
Propyl-paraben	0.02 g
Distilled water for injection	10.0 ml

The above parabens, sodium metabisulfite and sodium chloride are dissolved in distilled water of half volume of the above with stirring at 80°C. The solution thus obtained is cooled to 40°C, and the active compound of this invention and further polyethylene glycol and polyoxyethylene sorbitan monooleate are dissolved in the above solution. To the solution is added distilled water for injection to adjust to the desired volume, and the solution is sterilized by filtering with an appropriate filter paper to give an injection preparation.

Reference Example 1

To a solution of 1,2,3,4-tetrahydroquinoline (28.7 g) in acetone (400 ml) and water (200 ml) is added potassium carbonate (38.8 g), and thereto is added p-nitrobenzoyl chloride (40 g) under ice-cooling and the mixture is stirred at room temperature overnight. To the reaction mixture is added a suitable amount of water. The precipitated crystal is collected by filtration and dried to give 1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline (40.8 g) as white powder, m.p. 86 - 88°C.

Reference Example 2

To a solution of 10 % Pd-C (5 g) in ethanol (500 ml) is added 1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline (53.4 g) and the mixture is subjected to catalytic reduction at ordinary temperature under atmospheric pressure of hydrogen. After the reduction, 10 % Pd-C is removed by filtration, and the filtrate is concentrated under reduced pressure to give 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (46.7 g) as yellow powder, m.p. 185 - 188°C.

Reference Example 3

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 1.

1-(3-Nitrobenzoyl)-1,2,3,4-tetrahydroquinoline,  
white powder, m.p. 134 - 136°C

1-(2-Nitrobenzoyl)-1,2,3,4-tetrahydroquinoline,

yellow powder, m.p. 152 - 154°C

3-Methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydro-  
quinoline, yellow powder, m.p. 109 - 110°C

4-Methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydro-  
quinoline, yellow powder, m.p. 134 - 136°C

2-Methyl-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydro-  
quinoline, yellow powder, m.p. 143 - 145°C

1-(4-Nitrobenzoyl)-2,3,4,5-tetrahydro-1H-  
benzazepine, yellow powder, m.p. 143 - 145°C

1-(3-Methyl-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-  
benzazepine, white powder, m.p. 100 - 102°C

1-(3-Methoxy-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-  
benzazepine, yellow powder, m.p. 146 - 148°C

1-(4-Nitrobenzoyl)-1,2,3,4,5,6-hexahydrobenz-  
azocine, white powder, m.p. 83 - 85°C

1-(4-Nitrobenzoyl)-3,4-dihydro-2H-1,4-benzoxazine,  
yellow powder, m.p. 167 - 169°C

1-(4-Nitrobenzoyl)-1,2,3,5-tetrahydro-4,1-  
benzoxazepine, yellow powder, m.p. 196 - 198°C

1-(4-Nitrobenzoyl)-4-methyl-1,2,3,4-tetrahydro-  
quinoxaline, brown powder

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 3.03 (3H, s), 3.54 (2H, t,  $J=5.7$   
Hz), 4.06 (2H, t,  $J=5.7$  Hz), 6.2-6.5 (2H, m), 6.70 (1H, d,  
 $J=8.2$  Hz), 6.9-7.1 (1H, m), 7.54 (2H, d,  $J=8.8$  Hz), 8.13  
(2H, d,  $J = 8.8$  Hz)

1-(4-Nitrobenzoyl)-5-methyl-2,3,4,5-tetrahydro-1H-

1,5-benzodiazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.7-2.0 (1H, m), 2.0-2.3 (1H, m), 2.8-3.0 (1H, m), 2.98 (3H, s), 3.0-3.2 (1H, m), 3.4-3.6 (1H, m), 4.6-4.8 (1H, m), 6.5-6.7 (2H, m), 6.94 (1H, d,  $J=8.1$  Hz), 7.1-7.2 (1H, m), 7.33 (2H, d,  $J=8.9$  Hz), 7.97 (2H, d,  $J=8.9$  Hz)

1-(4-Nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, brown oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.44 (3H, s), 3.0-3.3 (3H, m), 3.77 (1H, d,  $J=13.7$  Hz), 4.06 (1H, d,  $J=13.6$  Hz), 4.9-5.1 (1H, m), 6.59 (1H, d,  $J=7.7$  Hz), 6.97 (1H, t,  $J=7.6$  Hz), 7.15 (1H, t,  $J=7.4$  Hz), 7.2-7.5 (3H, m), 8.03 (2H, d,  $J=8.8$  Hz)

1-(3-Methoxy-4-nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 146 - 148°C

1-(4-Nitrobenzoyl)-4-n-propyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 131 - 133°C

1-(4-Nitrobenzoyl)-5-chloro-1,2,3,4-tetrahydroquinoline, white powder, m.p. 134 - 136°C

1-(4-Nitrobenzoyl)-6-methoxy-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 149 - 151°C

1-(4-Nitrobenzoyl)-6-methyl-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 109 - 110°C

1-(4-Nitrobenzoyl)-7-methoxy-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 139 - 141°C

1-(4-Nitrobenzoyl)-3-(4-methyl-1-piperazinyl)-  
1,2,3,4-tetrahydroquinoline, yellow amorphous  
 $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.29 (3H, s), 2.35-3.20 (11H, m), 3.86-4.15 (2H, m), 6.48-6.63 (1H, m), 6.89 (1H, t,  $J=7.4$  Hz), 7.05 (1H, t,  $J=7.4$  Hz), 7.22 (1H, d,  $J=7.4$  Hz), 7.52 (2H, d,  $J=8.8$  Hz), 8.11 (2H, d,  $J=8.8$  Hz)

1-(4-Nitrobenzoyl)-3-(1-pyrrolidinyl)-1,2,3,4-tetrahydroquinoline, yellow amorphous  
 $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.70-1.95 (4H, m), 2.52-3.30 (7H, m), 3.80-4.22 (2H, m), 6.52 (1H, brs), 6.88 (1H, t,  $J=7.6$  Hz), 6.96-7.11 (1H, m), 7.20 (2H, d,  $J=7.6$  Hz), 7.54 (2H, d,  $J=8.8$  Hz), 8.12 (2H, d,  $J=8.8$  Hz)

1-(4-Nitrobenzoyl)-4-oxo-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 189 - 190°C

1-(4-Nitrobenzoyl)-3-hydroxymethyl-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 97 - 100°C

1-(4-Nitrobenzoyl)-3-ethoxycarbonyl-1,2,3,4-tetrahydroquinoline, pale yellow powder, m.p. 162 - 163°C

1-(4-Nitrobenzoyl)-4-dimethylamino-1,2,3,4-tetrahydroquinoline, light brown oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.80-2.02 (1H, m), 2.20-2.50 (7H, m), 3.47 (1H, t,  $J=4.9$  Hz), 3.70-3.88 (1H, m), 4.06-4.25 (1H, m), 6.46 (1H, d,  $J=7.5$  Hz), 6.89 (1H, t,  $J=7.5$  Hz), 7.05 (1H, t,  $J=7.5$  Hz), 7.34 (1H, d,  $J=7.5$  Hz), 7.50 (2H, d,  $J=7.0$  Hz), 8.10 (2H, d,  $J=7.0$  Hz)

Reference Example 4



Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 2.

1-(3-Aminobenzoyl)-1,2,3,4-tetrahydroquinoline,  
white powder, m.p. 128 - 130°C

1-(2-Aminobenzoyl)-1,2,3,4-tetrahydroquinoline,  
yellow powder

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ : 2.01 (2H, quint, J=6.6 Hz), 2.81 (2H, t, J=6.6 Hz), 3.86 (2H, t, J=6.4 Hz), 4.6-4.8 (2H, m), 6.43 (1H, t, J=7 Hz), 6.66 (1H, d, J=8 Hz), 6.79 (1H, dd, J=1.4 Hz, J=7.6 Hz), 6.8-7.2 (5H, m)

3-Methyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 197 - 200°C

4-Methyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 197 - 199°C

2-Methyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow powder, m.p. 204 - 206°C

1-(4-Aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow powder, m.p. 172 - 174°C

1-(3-Methyl-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 156 - 158°C

1-(3-Methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 165 - 167°C

1-(4-Aminobenzoyl)-1,2,3,4,5,6-hexahydrobenzazocine, white powder, m.p. 177 - 179°C

1-(4-Aminobenzoyl)-3,4-dihydro-2H-1,4-benzoxazine,

white powder, m.p. 192 - 194°

1-(4-Aminobenzoyl)-1,2,3,5-tetrahydro-4,1-benz-oxazepine, yellow powder, m.p. 196 - 198°C

1-(4-Aminobenzoyl)-4-methyl-1,2,3,4-tetrahydro-quinoxaline, yellow powder, m.p. 210 - 212°C

1-(4-Aminobenzoyl)-5-methyl-2,3,4,5-tetrahydro-1H-1,5-benzodiazepine, white powder, m.p. 159 - 161°C

1-(4-Aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, brown powder, m.p. 169 - 171°C

1-(3-Methoxy-4-aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.41 (3H, s), 2.9-3.2 (3H, m), 3.61 (3H, s), 3.6-4.2 (4H, m), 4.8-5.2 (1H, m), 6.38 (1H, d,  $J=8.1$  Hz), 6.6-6.8 (3H, m), 6.9-7.2 (2H, m), 7.2-7.4 (1H, m)

1-(4-Aminobenzoyl)-4-n-propyl-2,3,4,5-tetrahydro-1H-1,4-benzazepine, brown powder, m.p. 151 - 153°C

1-(4-Aminobenzoyl)-5-chloro-1,2,3,4-tetrahydro-quinoline, white powder, m.p. 174 - 175°C

1-(4-Aminobenzoyl)-6-methoxy-1,2,3,4-tetrahydro-quinoline, pale yellow powder, m.p. 159 - 160°C

1-(4-Aminobenzoyl)-6-methyl-1,2,3,4-tetrahydro-quinoline, white powder, m.p. 145 - 146°C

1-(4-Aminobenzoyl)-7-methoxy-1,2,3,4-tetrahydro-quinoline, pale yellow powder, m.p. 150 - 151°C

1-(4-Aminobenzoyl)-3-(4-methyl-1-piperazinyl)-1,2,3,4-tetrahydroquinoline, light beige powder, m.p. 157 -

159°C

1-(4-Aminobenzoyl)-3-(1-pyrrolidinyl)-1,2,3,4-tetrahydroquinoline, pale yellow powder, m.p. 173 - 174.5°C

1-(4-Aminobenzoyl)-2,3-dihydro-4(1H)-quinolinone, pale yellow powder, m.p. 178 - 180°C

1-(4-Aminobenzoyl)-3-hydroxymethyl-1,2,3,4-tetrahydroquinoline, white powder, m.p. 179 - 181°C

1-(4-Aminobenzoyl)-3-ethoxycarbonyl-1,2,3,4-tetrahydroquinoline, pale yellow amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.21 (3H, t,  $J=7.1$  Hz), 3.00-3.24 (3H, m), 3.70-4.30 (6H, m), 6.48 (2H, d,  $J=8.5$  Hz), 6.69 (1H, d,  $J=7.9$  Hz), 6.77-7.30 (5H, m)

1-(4-Aminobenzoyl)-4-dimethylamino-1,2,3,4-tetrahydroquinoline, brown oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.83-2.05 (1H, m), 2.13-2.30 (1H, m), 2.34 (6H, m), 3.55-3.83 (2H, m), 3.89 (1H, brs), 3.97-4.18 (1H, m), 6.47 (2H, d,  $J=7.0$  Hz), 6.68 (1H, d,  $J=7.9$  Hz), 6.85-7.05 (2H, m), 7.20 (2H, d,  $J=7.0$  Hz), 7.37 (1H, d,  $J=7.4$  Hz)

#### Reference Example 5

To terephthalic acid monomethyl ester (15 g) is added thionyl chloride (100 ml) and the mixture is refluxed for 2 hours. The thionyl chloride is distilled off under reduced pressure to give terephthalic acid chloride monomethyl ester. Separately, to a solution of 1,2,3,4-tetrahydroquinoline (14.4 g) in dichloromethane (200 ml) is

added triethylamine (16.9 g) and further thereto is added slowly terephthalic acid chloride monomethyl ester obtained above under ice-cooling. Then, the mixture is stirred at room temperature for 1 hour. After completion of the reaction, water is added to the reaction mixture. The mixture is extracted with dichloromethane and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane) to give 1-(4-methoxycarbonylbenzoyl)-1,2,3,4-tetrahydroquinoline (22.7 g) as white powder, m.p. 72 - 74°C.

#### Reference Example 6

To a solution of 1-(4-methoxycarbonylbenzoyl)-1,2,3,4-tetrahydroquinoline (22.7 g) in methanol (300 ml) is added 5 % aqueous sodium hydroxide solution (150 ml) and the mixture is refluxed for 2 hours. Methanol is distilled off under reduced pressure and the resulting residue is acidified with diluted hydrochloric acid, extracted with diethyl ether, and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting crystal is collected by filtration to give 1-(4-carboxybenzoyl)-1,2,3,4-tetrahydroquinoline (13.2 g) as white powder, m.p. 181 - 183°C.

#### Reference Example 7

Using the suitable starting materials, the

following compounds are obtained in the same manner as in Reference Example 1.

5-Dimethylamino-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow powder, m.p. 139 - 142°C

5-Dimethylamino-1-(3-methoxy-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 139 - 141°C

4-(N-Methyl-N-ethylamino)-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, pale yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.11 (3H, t,  $J=7.1$  Hz), 1.90-2.25 (2H, m), 2.30 (3H, s), 2.57 (2H, q,  $J=7.1$  Hz), 3.55-3.85 (2H, m), 4.00-4.21 (1H, m), 6.35-6.60 (1H, m), 6.80-6.98 (1H, t,  $J=7.9$  Hz), 7.00-7.15 (1H, m), 7.33-7.60 (3H, m), 8.10 (2H, d,  $J=8.8$  Hz)

4-Dimethylamino-1-(3-methoxy-4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, brown oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.80-2.05 (1H, m), 2.33 (6H, s), 2.30-2.50 (1H, m), 3.40-3.52 (1H, m), 3.78 (3H, s), 3.70-3.88 (1H, m), 4.04-4.24 (1H, m), 6.52 (1H, d,  $J=8.2$  Hz), 6.85-7.13 (4H, m), 7.28-7.38 (1H, m), 7.71 (1H, d,  $J=8.2$  Hz)

1-(4-Nitrobenzoyl)-4-ethyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.16 (3H, t,  $J=7.1$  Hz), 2.5-2.7 (2H, m), 3.0-3.3 (3H, m), 3.98 (2H, q,  $J=14$  Hz), 4.8-5.0 (1H, m), 6.59 (1H, d,  $J=7.7$  Hz), 6.96 (1H, t,  $J=7.7$  Hz),

7.14 (1H, t, J=7.4 Hz), 7.2-7.4 (3H, m), 8.02 (2H, d, J=8.8 Hz)

1-(4-Nitrobenzoyl)-4-isopropyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 222 - 223°C

1-(4-Nitrobenzoyl)-4-cyclohexyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, brown oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.0-1.5 (5H, m), 1.5-2.1 (5H, m), 2.4-2.7 (1H, m), 2.9-3.3 (3H, m), 3.94 (2H, s), 4.9-5.1 (1H, m), 6.57 (1H, d, J=7.7 Hz), 6.8-7.0 (1H, m), 7.0-7.2 (1H, m), 7.2-7.4 (3H, m), 8.01 (2H, d, J=8.8 Hz)

1-(4-Nitrobenzoyl)-5-methyl-1,2,3,4,5,6-hexahydro-1,5-benzodiazocine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.5-2.1 (2H, m), 2.40 (3H, s), 2.3-2.6 (1H, m), 2.8-3.2 (2H, m), 3.50 (1H, d, J=13.4 Hz), 3.84 (1H, d, J=13.4 Hz), 4.8-5.0 (1H, m), 7.0-7.3 (4H, m), 7.41 (2H, d, J=8.9 Hz), 8.00 (2H, d, J=8.9 Hz)

1-(4-Nitrobenzoyl)-1,2,3,4-tetrahydro-5,1-benzoxazepine, white powder, m.p. 144.5 - 145.5°C

1-(2-Nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 177 - 180°C

1-(3-Nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 145 - 146°C

6-Fluoro-1-(4-nitrobenzoyl)-1,2,3,4-tetrahydroquinoline, yellow needles, m.p. 145 - 146°C

#### Reference Example 8

Using the suitable starting materials, the

following compounds are obtained in the same manner as in Reference Example 2.

5-Dimethylamino-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 120 - 122°C

5-Dimethylamino-1-(3-methoxy-4-amino)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 121 - 123°C

4-(N-Methy-N-ethylamino)-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, orange amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.11 (3H, t,  $J=7.1$  Hz), 1.90-2.20 (2H, m), 2.28 (3H, s), 2.26 (2H, q,  $J=7.1$  Hz), 3.60-4.25 (5H, m), 6.48 (2H, d,  $J=8.5$  Hz), 6.69 (1H, d,  $J=7.9$  Hz), 6.80-7.05 (2H, m), 7.24 (2H, d,  $J=8.5$  Hz), 7.46 (1H, d,  $J=6.2$  Hz)

4-Dimethylamino-1-(3-methoxy-4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, pale yellow amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.83-2.04 (1H, m), 2.15-2.32 (1H, m), 2.33 (6H, s), 3.50-3.82 (2H, m), 3.64 (3H, s), 3.95-4.18 (3H, m), 6.50 (1H, d,  $J=7.9$  Hz), 6.65 (1H, dd,  $J=7.9$  Hz, 1.1 Hz), 6.78-7.03 (4H, m), 7.34 (1H, dd,  $J=7.5$  Hz, 1.5 Hz)

1-(4-Aminobenzoyl)-4-ethyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 186 - 188°C

1-(4-Aminobenzoyl)-4-isopropyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 191 - 192°C

1-(4-Aminobenzoyl)-4-cyclohexyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 149.5 - 150.5°C

1-(4-Aminobenzoyl)-5-methyl-1,2,3,4,5,6-hexahydro-1,5-benzodiazocine, yellow powder, m.p. 143 - 145°C

1-(4-Aminobenzoyl)-1,2,3,4-tetrahydro-5,1-benzoxazepine, yellow powder, m.p. 163.5 - 164.5°C

1-(2-Aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, yellow powder, m.p. 144 - 146°C

1-(3-Aminobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine, white powder, mp. 153 - 155°C

6-Fluoro-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 160.5 - 161.5°C

#### Reference Example 9

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 1.

1-(2-Chloro-4-nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.40 (3H, s), 2.96-3.33 (3H, m), 3.60-3.79 (1H, m), 3.96-4.23 (1H, m), 4.70-4.91 (1H, m), 6.80-7.43 (5H, m), 7.80-7.99 (1H, m), 8.08-8.21 (1H, m)

1-(3-Methyl-4-nitrobenzoyl)-4-methyl-2,3,4,5-tetrahydro-1H-1,4-benzodiazepine

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.43 (3H, s), 2.48 (3H, s), 2.92-3.28 (3H, m), 3.91 (2H, AB-q,  $J=13.9$  Hz, 45.5 Hz), 4.77-5.01 (1H, m), 6.54-6.70 (1H, m), 6.88-7.37 (5H, m), 7.62-7.78 (1H, m)

5-Dimethylamino-1-(2-chloro-4-nitrobenzoyl)-



## 2,3,4,5-tetrahydro-1H-benzazepine

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.23-2.57 (10H, m), 2.68-5.15 (3H, m), 6.79-7.45 (4H, m), 7.49-8.39 (3H, m)

5-Oxo-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (ethyl acetate/n-hexane), m.p. 147 - 148°C

5-Hydroxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder (ethyl acetate/n-hexane), m.p. 148 - 150°C

5-Methoxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.47-2.48 (4H, m), 2.70-3.10 (1H, m), 3.26-3.64 (3H, m), 4.29-5.12 (2H, m), 6.60 (1H, d,  $J=7.7$  Hz), 6.88-7.67 (5H, m), 7.92-8.12 (2H, m)

5-Ethoxycarbonylmethoxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 107 - 108°C (recrystallized from ethyl acetate/n-hexane)

5-(4-Bromobutoxy)-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.49-2.55 (8H, m), 2.72-3.07 (1H, m), 3.24-3.77 (4H, m), 4.40-5.15 (2H, m), 6.53-6.66 (1H, m), 6.91-7.06 (1H, m), 7.07-7.80 (4H, m), 7.94-8.13 (2H, m)

5-(4-Dimethylaminobutoxy)-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.51-1.88 (6H, m), 2.23-2.61

(4H, m), 2.27 (3H, s), 2.35 (3H, s), 2.74-3.14 (1H, m),  
3.55-3.77 (2H, m), 4.48-5.11 (2H, m), 6.54-6.66 (1H, m),  
6.91-7.04 (1H, m), 7.06-7.80 (4H, m), 7.93-8.11 (2H, m)

5-[4-(Phthalimid-1-yl)propoxy-1-(4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.48-2.56 (6H, m), 2.71-3.05  
(1H, m), 3.40-4.05 (4H, m), 4.47-5.11 (2H, m), 6.50-6.64  
(1H, m), 6.84-7.03 (1H, m), 7.03-7.20 (1H, m), 7.20-7.57  
(2H, m), 7.57-7.93 (5H, m), 7.97-8.20 (2H, m)

5-Chloro-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-  
benzazepine, light brown powder

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.75-3.3 (4H, m), 4.6-6.25 (3H,  
m), 6.45-6.7 (1H, m), 6.8-7.5 (4H, m), 7.55-7.7 (1H, m),  
7.9-8.1 (2H, m)

5-Oxo-1-(2-chloro-4-nitrobenzoyl)-2,3,4,5-tetra-  
hydro-1H-benzazepine, pale yellow amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.95-2.45 (2H, m), 2.94 (1H, t,  
 $J=6$  Hz), 3.05-5.3 (2H, m), 6.96-7.1 (1H, m), 7.12-7.5 (3H,  
m), 7.75-7.85 (1H, m), 7.95-8.1 (1H, m), 8.14 (1H, s)

4-Dimethylaminomethyl-1-(4-nitrobenzoyl)-1,2,3,4-  
tetrahydroquinoline, white powder, m.p. 117 - 119°C

3-Dimethylamino-1-(4-nitrobenzoyl)-2,3,4,5-  
tetrahydro-1H-benzazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.5-1.7 (1H, m), 2.1-2.4 (1H,  
m), 2.42 (6H, s), 2.6-2.7 (1H, m), 2.8-3.0 (3H, m), 5.1-5.3  
(1H, m), 6.62 (1H, d,  $J=7.8$  Hz), 6.95 (1H, t,  $J=7.7$  Hz),

7.14 (1H, t, J=7.5 Hz), 7.2-7.4 (3H, m), 8.00 (2H, d, J=8.9 Hz)

3-Dimethylamino-1-(3-methoxy-4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.5-1.7 (1H, m), 2.0-2.3 (1H, m), 2.41 (6H, s), 2.5-2.8 (1H, m), 2.8-3.0 (3H, m), 3.75 (3H, s), 5.1-5.3 (1H, m), 6.6-6.8 (2H, m), 6.9-7.3 (4H, m), 7.59 (1H, d, J=8.3 Hz)

4-(4-Nitrobenzoyl)-3,4-dihydro-2H-1,4-benzo-  
thiazine, yellow powder, m.p. 180 - 182°C

5-(4-Nitrobenzoyl)-2,3,4,5-tetrahydro-1,5-  
benzothiazepine, yellow powder, m.p. 162 - 163°C

#### Reference Example 10

Using the suitable starting materials, the  
following compounds are obtained in the same manner as in  
Reference Example 2.

1-(2-Chloro-4-aminobenzoyl)-4-methyl-2,3,4,5-  
tetrahydro-1H-1,4-benzodiazepine, white powder  
(recrystallized from methanol/diethyl ether), m.p. 194.5 -  
195.5°C

1-(3-Methyl-4-aminobenzoyl)-4-methyl-2,3,4,5-  
tetrahydro-1H-1,4-benzodiazepine

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.01 (3H, s), 2.41 (3H, s),  
2.82-3.21 (3H, m), 3.50-4.21 (4H, m), 4.78-5.14 (1H, m),  
6.24-6.40 (1H, m), 6.59-6.82 (2H, m), 6.90-7.18 (3H, m),  
7.19-7.34 (1H, m)

5-Dimethylamino-1-(2-chloro-4-aminobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, white powder  
(recrystallized from dichloromethane/diethyl ether), m.p.  
162 - 164°C

5-Dimethylamino-1-(2-methoxy-4-aminobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine (recrystallized from  
methanol/diethyl ether)

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.23-2.80 (11H, m), 2.90-3.38  
(1H, m), 3.50-5.19 (6H, m), 5.87-6.41 (2H, m), 6.65-7.56  
(5H, m)

5-Methoxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-  
benzazepine, white powder (recrystallized from ethyl  
acetate/n-hexane), m.p. 154 - 155°C

5-Ethoxycarbonylmethoxy-1-(4-aminobenzoyl)-2,3,4,5-  
tetrahydro-1H-benzazepine, white powder (recrystallized from  
ethyl acetate/n-hexane), m.p. 231 - 232°C

5-(4-Dimethylaminobutoxy)-1-(4-aminobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, colorless oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.47-1.83 (6H, m), 1.83-2.54  
(4H, m), 2.29 (6H, s), 2.61-3.00 (1H, m), 3.36-3.76 (2H, m),  
4.35-5.20 (2H, m), 6.27-6.48 (2H, m), 6.57-6.76 (1H, m),  
6.90-7.61 (5H, m)

5-[4-(Phthalimid-1-yl)propoxy]-1-(4-aminobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.30-2.47 (6H, m), 2.57-3.01  
(1H, m), 3.30-4.06 (4H, m), 4.34-5.20 (2H, m), 6.30-6.53

(2H, m), 6.57-6.78 (1H, m), 6.87-7.57 (5H, m), 7.62-7.76 (2H, m), 7.76-7.97 (2H, m)

5-Chloro-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.35-4.3 (7H, m), 4.55-6.7 (2H, m), 6.3-6.55 (2H, m), 6.6-6.8 (1H, m), 6.85-7.45 (5H, m)

5-Oxo-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, pale yellow amorphous

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.95-2.35 (2H, m), 2.89 (2H, t,  $J=6.3$  Hz), 3.0-5.3 (4H, m), 6.35-6.47 (2H, m), 6.72-6.83 (1H, m), 7.0-7.15 (2H, m), 7.18-7.32 (2H, m), 7.81-7.93 (1H, m)

5-Oxo-1-(2-chloro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.85-2.3 (2H, m), 2.87 (2H, t,  $J=6.2$  Hz), 3.1-4.75 (4H, m), 6.15-7.5 (6H, m), 7.65-7.9 (1H, m)

4-Dimethylaminomethyl-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline, white powder, m.p. 123 - 125°C

3-Dimethylamino-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 175 - 177°C

3-Dimethylamino-1-(3-methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.5-1.7 (1H, m), 2.1-2.3 (1H, m), 2.3-2.6 (1H, m), 2.40 (6H, s), 2.7-3.0 (3H, m), 3.60 (3H, s), 3.8-4.0 (2H, br), 5.2-5.4 (1H, m), 6.37 (1H, d,

J=8.2 Hz), 6.5-6.8 (3H, m), 6.9-7.4 (3H, m)

4-(4-Aminobenzoyl)-3,4-dihydro-2H-1,4-benzothiazine, yellow powder, m.p. 207 - 210°C

5-(4-Aminobenzoyl)-2,3,4,5-tetrahydro-1,5-benzothiazepine, yellow powder, m.p. 193 - 195°C

Reference Example 11

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 1.

5-Carbamoyloxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 243 - 244°C

(recrystallized from ethyl acetate/diisopropyl ether)

5-Methylaminocarbonyloxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 207 - 208°C (recrystallized from ethyl acetate/n-hexane)

5-Dimethylaminocarbonyloxy-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 155 - 156°C (recrystallized from ethyl acetate/diisopropyl ether/n-hexane)

5-Methylidenyl-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless prisms, m.p. 133.5 - 134°C (recrystallized from ethyl acetate/diisopropyl ether)

5-Oxo-6-methyl-1-(2-chloro-4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless prisms, m.p. 90 - 92°C (recrystallized from ethanol)

1-(4-Nitrobenzoyl)-1,2,3,5-tetrahydro-4,1-

benzothiazepine, yellow powder, m.p. 185 - 187°C

(recrystallized from dichloromethane/diethyl ether)

5-Dimethylamino-1-(2-dimethylamino-4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, yellow powder, m.p. 123 -  
125°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-1-(4-nitrobenzoyl)-2,3,4,5-tetrahydro-1H-1,4-  
benzodiazepine, white powder, m.p. 201.5 - 202.5°C  
(recrystallized from diethyl ether/dichloromethane)

5-Oxo-4-methyl-1-(4-nitrobenzoyl)-2,3,4,5-  
tetrahydro-1H-1,4-benzodiazepine, white powder, m.p. 136 -  
138°C (recrystallized from diethyl ether/dichloromethane)

5-Dimethylamino-1-(3-methyl-4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ : 1.16-3.18 (11H, m), 2.18 (3H,  
s), 3.40-5.15 (2H, m), 6.50-7.68 (6H, m), 7.70-7.84 (1H, m)

5-Dimethylamino-1-(2-methyl-4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, colorless amorphous

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ : 1.19-2.86 (11H, m), 2.20 (3H,  
s), 2.94-3.24 (1H, m), 3.36-5.18 (1H, m), 6.49-8.20 (7H, m)

5-Dimethylamino-1-(2-fluoro-4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

<sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ : 1.21-2.66 (10H, m), 2.66-5.11  
(3H, m), 6.63-8.25 (7H, m)

5-Dimethylamino-1-(3-fluoro-4-nitrobenzoyl)-  
2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 152 -  
152.5°C (recrystallized from chloroform/diethyl ether)

Reference Example 12

Using the suitable starting materials, the following compounds are obtained in the same manner as in Reference Example 2.

5-Carbamoyloxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 215 - 216°C (recrystallized from ethyl acetate/n-hexane)

5-Methylaminocarbonyloxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 192 - 195°C (recrystallized from ethyl acetate/n-hexane)

5-Dimethylaminocarbonyloxy-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 228 - 230°C (recrystallized from ethyl acetate/diisopropyl ether)

5-Methyl-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 155 - 156°C (recrystallized from ethyl acetate/n-hexane)

5-Oxo-6-methyl-1-(2-chloro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 193 - 195°C (recrystallized from ethanol)

1-(4-Aminobenzoyl)-1,2,3,5-tetrahydro-4,1-benzothiazepine, white powder, m.p. 179 - 180°C (recrystallized from dichloromethane/diethyl ether)

5-Dimethylamino-1-(2-dimethylamino-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 163 - 165°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-



benzazepine, yellow powder, m.p. 195 - 197°C (recrystallized from diethyl ether/dichloromethane)

5-Oxo-4-methyl-1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-1,4-benzazepine, yellow powder, m.p. 190 - 192°C (recrystallized from diethyl ether/dichloromethane)

5-Dimethylamino-1-(2-ethoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 111 - 114°C (recrystallized from diethyl ether)

5-Dimethylamino-1-(3-methyl-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, yellow oil

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 0.66-2.56 (14H, m), 2.93-5.22 (4H, m), 6.23-7.80 (7H, m)

5-Dimethylamino-1-(2-methyl-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 154 - 156°C (recrystallized from methanol/diethyl ether)

5-Dimethylamino-1-(2-fluoro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 161 - 163°C (recrystallized from dichloromethane/diethyl ether)

5-Dimethylamino-1-(3-fluoro-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, white powder, m.p. 156 - 157°C (recrystallized from methanol/diethyl ether)

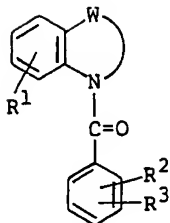
5-Oxo-1-(2-methoxy-4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine, colorless prisms, m.p. 160 - 160.5°C (recrystallized from methanol/diethyl ether)

#### Example 1

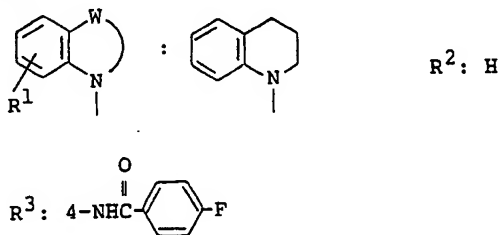
To a solution of 1,2,3,4-tetrahydroquinoline (28.7

g) in acetone (400 ml) and water (200 ml) is added potassium carbonate (38.8 g) and further thereto is added 4-benzoyl-aminobenzoyl chloride (56 g) under ice-cooling. The mixture is stirred at room temperature overnight. Water is added to the reaction mixture, and the mixture is extracted with dichloromethane. The extract is dried over magnesium sulfate, and the solvent is distilled off under reduced pressure. The resulting residue is purified by silica gel column chromatography and recrystallized from methanol to give 1-[4-(benzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (57 g) as white powder, m.p. 202.5 - 203.5°C.

Using the suitable starting materials, the compounds as shown in the following Table 1 are obtained in the same manner as in Example 1.

Table 1

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**Example 2****Structure**

Crystalline form: Light yellow powder

Recrystallization solvent: Methanol

Melting Point: 198.5 - 199.5°C

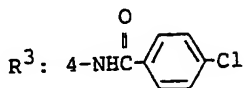
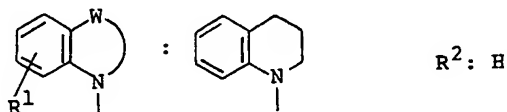
Form: Free

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Example 3

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

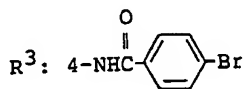
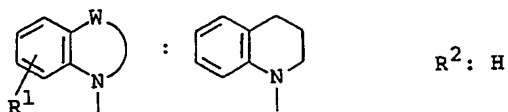
Melting Point: 200.5 - 201.5°C

Form: Free

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## Example 4

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

Melting Point: 206 - 207°C

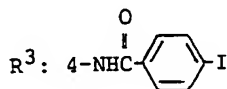
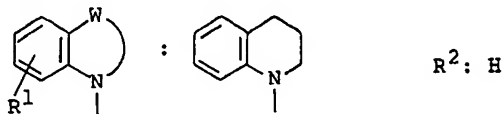
Form: Free

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Example 5

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

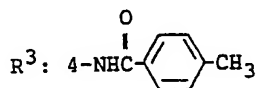
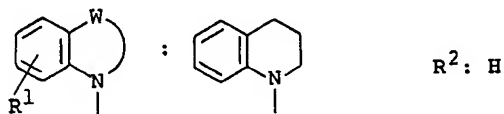
Melting Point: 216 - 217°C

Form: Free

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## Example 6

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 202 - 203°C

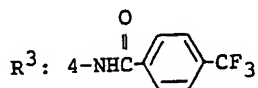
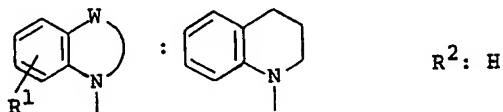
Form: Free

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Example 7

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

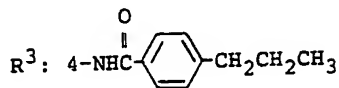
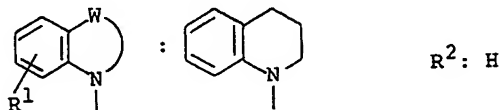
Melting Point: 212 - 213°C

Form: Free

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## Example 8

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 167.5 - 168.5°C

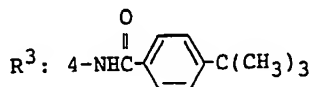
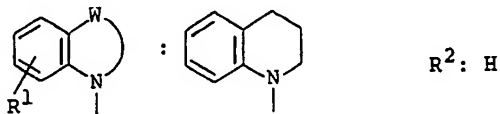
Form: Free

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Example 9

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

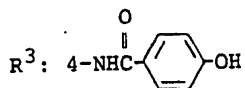
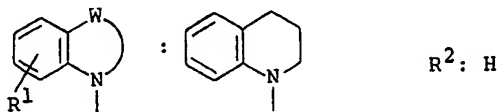
Melting Point: 205 - 206°C

Form: Free

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## Example 10

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: &gt;300°C

NMR analysis: 1)

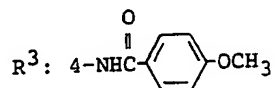
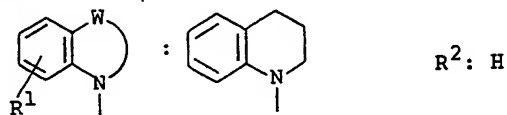
Form: Free

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Example 11

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

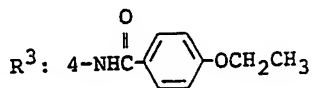
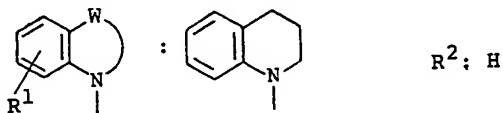
Melting Point: 176 - 177°C

Form: Free

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## Example 12

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 219 - 220°C

Form: Free

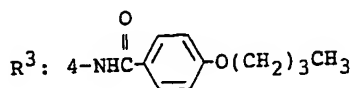
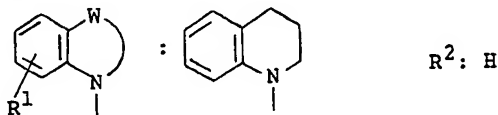
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Example 13

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

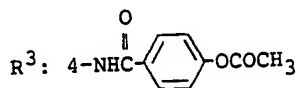
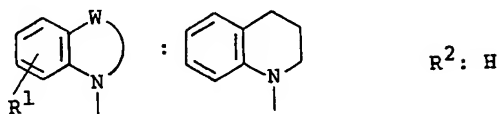
Melting Point: 193 - 194°C

Form: Free

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## Example 14

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 232 - 233°C

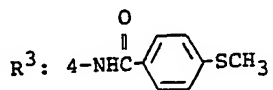
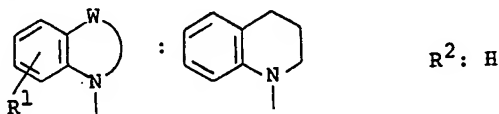
Form: Free

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Example 15

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

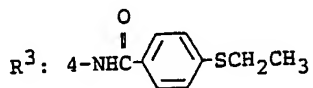
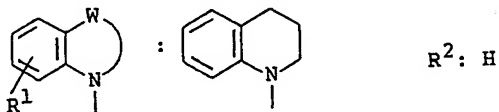
Melting Point: 209 - 210°C

Form: Free

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## Example 16

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 184.5 - 185.5°C

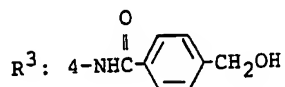
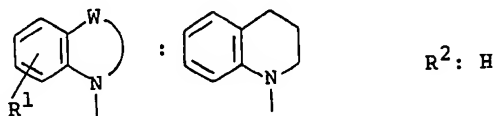
Form: Free

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Example 17

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

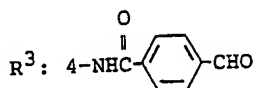
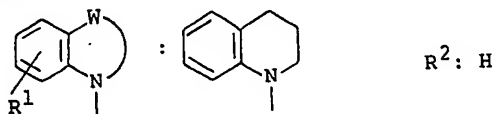
Melting Point: 224.5 - 225.5°C

Form: Free

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## Example 18

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 220.5 - 221.5°C

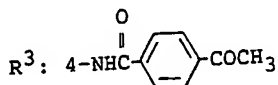
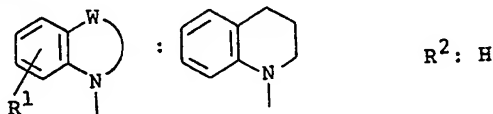
Form: Free

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Example 19

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

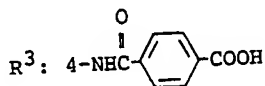
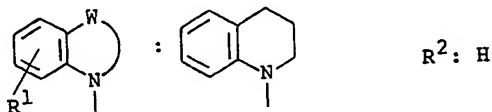
Melting Point: 231 - 232°C

Form: Free

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## Example 20

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: >300°C

NMR analysis: 2)

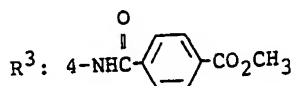
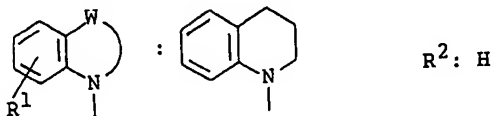
Form: Free

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Example 21

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

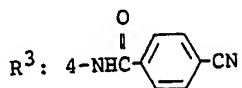
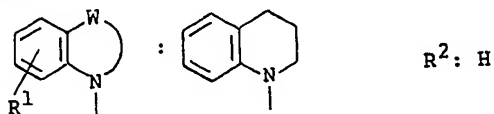
Melting Point: 208 - 209°C

Form: Free

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## Example 22

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 234.5 - 235.5°C

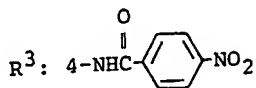
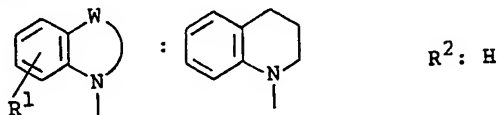
Form: Free

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Example 23

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

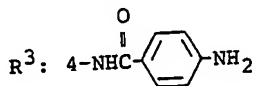
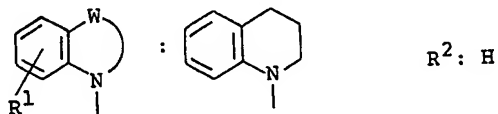
Melting Point: 263.5 - 264.5°C

Form: Free

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## Example 24

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 237 - 238°C

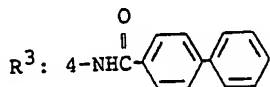
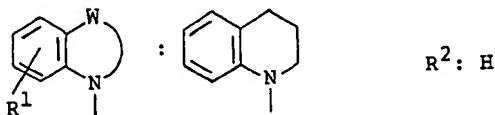
Form: Free

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Example 25

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

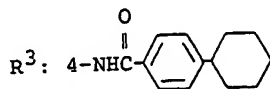
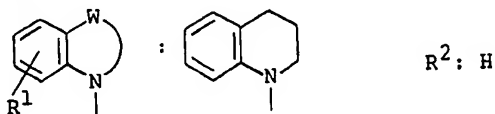
Melting Point: 234 - 235°C

Form: Free

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## Example 26

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 236.5 - 237.5°C

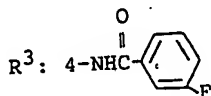
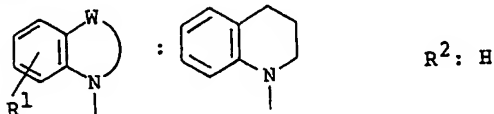
Form: Free

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Example 27

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

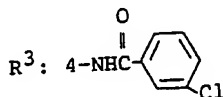
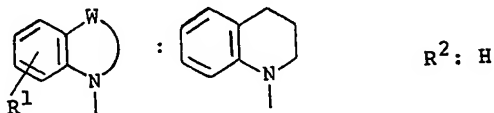
Melting Point: 206.5 - 207.5°C

Form: Free

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## Example 28

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 210 - 211°C

Form: Free

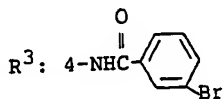
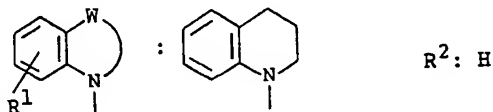
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Example 29

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

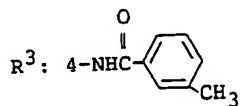
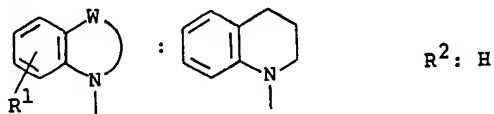
Melting Point: 210.5 - 211.5°C

Form: Free

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## Example 30

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 178 - 179°C

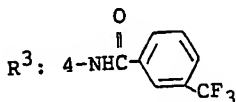
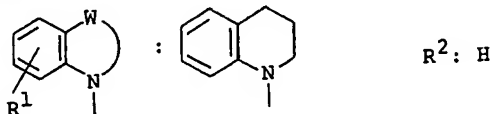
Form: Free

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Example 31

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

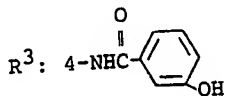
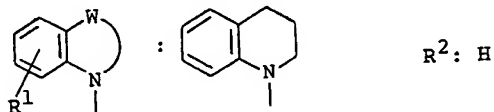
Melting Point: 192 - 193°C

Form: Free

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## Example 32

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 217 - 218°C

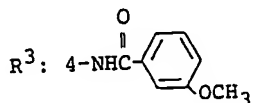
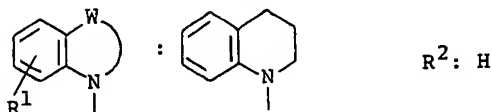
Form: Free

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Example 33

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

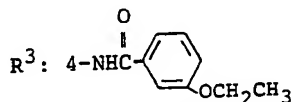
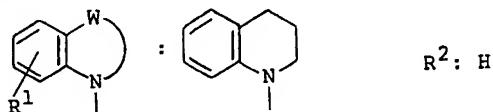
Melting Point: 143 - 144°C

Form: Free

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## Example 34

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 170.5 - 171.5°C

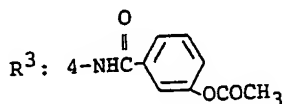
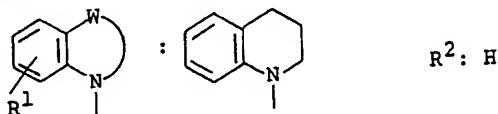
Form: Free

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Example 35

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

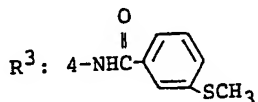
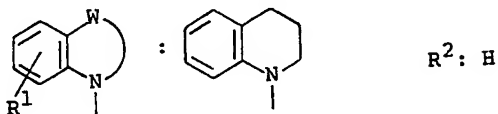
Melting Point: 169.5 - 170.5°C

Form: Free

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## Example 36

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 174.5 - 175.5°C

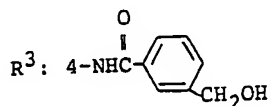
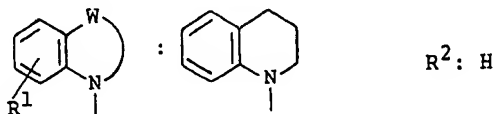
Form: Free

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Example 37

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

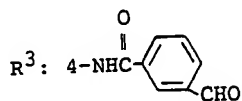
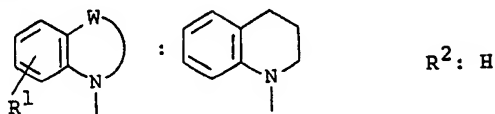
Melting Point: 148.5 - 149.5°C

Form: Free

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## Example 38

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 165 - 166°C

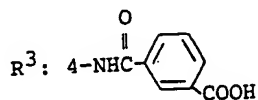
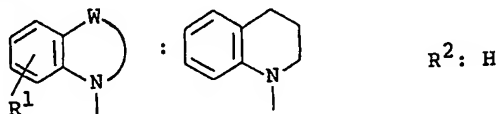
Form: Free

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Example 39

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

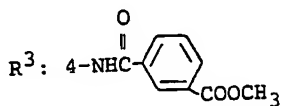
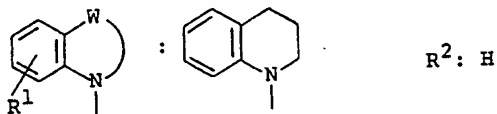
Melting Point: 243 - 244°C

Form: Free

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## Example 40

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 199 - 200°C

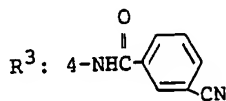
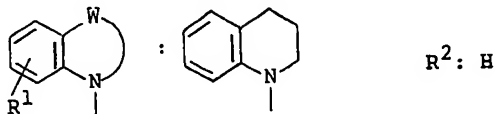
Form: Free

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Example 41

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

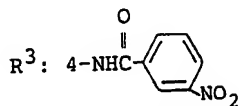
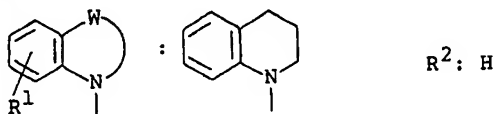
Melting Point: 232.5 - 233.5°C

Form: Free

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## Example 42

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 178.5 - 179.5°C

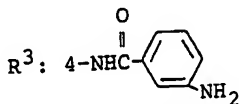
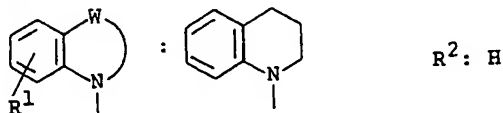
Form: Free

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Example 43

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

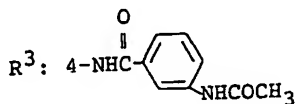
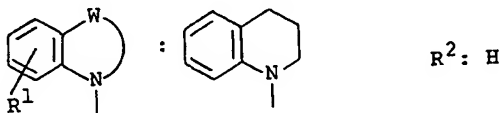
Melting Point: 205.5 - 206.5°C

Form: Free

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## Example 44

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 234 - 235°C

Form: Free

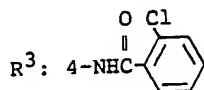
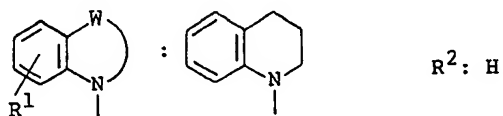
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Example 45

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

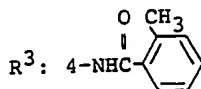
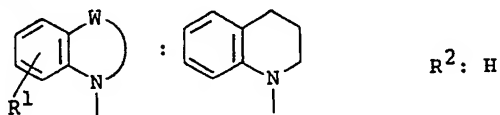
Melting Point: 225 - 226°C

Form: Free

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## Example 46

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 224 - 225°C

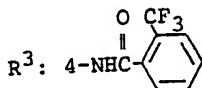
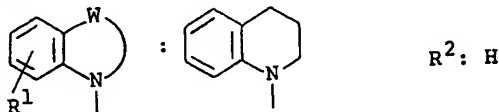
Form: Free

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Example 47

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

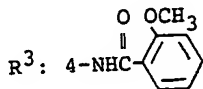
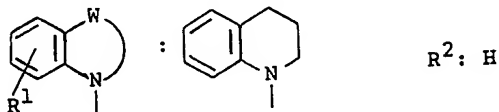
Melting Point: 236 - 237°C

Form: Free

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## Example 48

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

Melting Point: 175.5 - 176.5°C

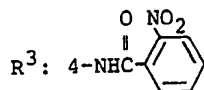
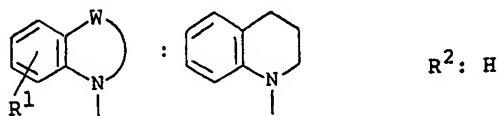
Form: Free

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Example 49

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

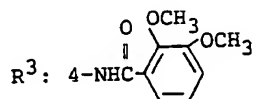
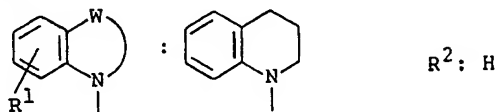
Melting Point: 231 - 232°C

Form: Free

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## Example 50

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

Melting Point: 204 - 205°C

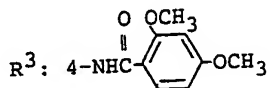
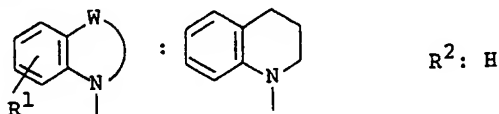
Form: Free

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Example 51

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

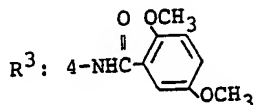
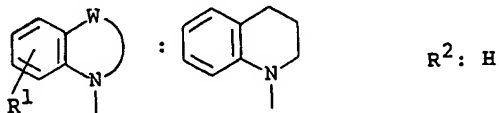
Melting Point: 190 - 191°C

Form: Free

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## Example 52

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 156 - 157°C

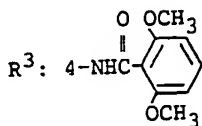
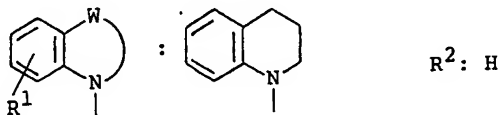
Form: Free

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Example 53

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

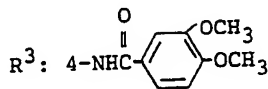
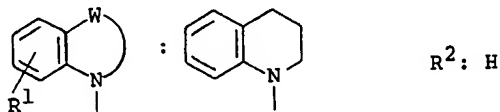
Melting Point: 200 - 201°C

Form: Free

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## Example 54

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 206 - 207°C

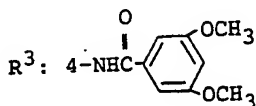
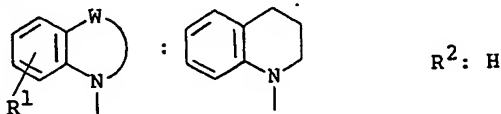
Form: Free

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Example 55

## Structure



Crystalline form: Colorless amorphous

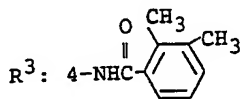
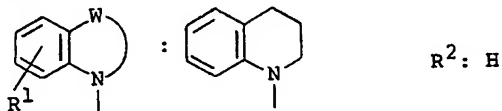
NMR analysis: 3)

Form: Free

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## Example 56

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 215.5 - 216.5°C

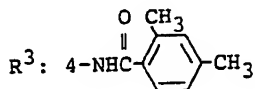
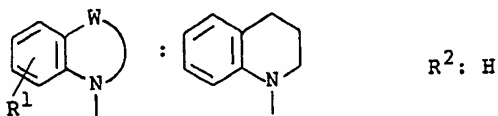
Form: Free

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Example 57

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

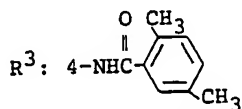
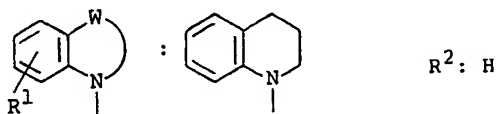
Melting Point: 189 - 190°C

Form: Free

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## Example 58

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 203.5 - 204.5°C

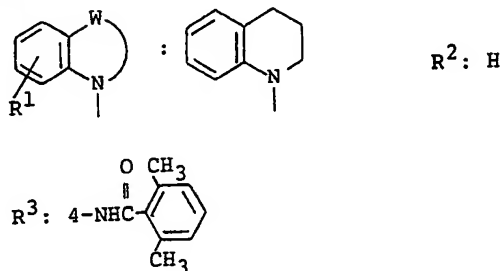
Form: Free

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Example 59

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

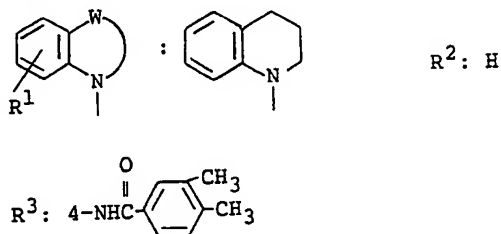
Melting Point: 254.5 - 255.5°C

Form: Free

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## Example 60

## Structure



Crystalline form: Brown powder

Recrystallization solvent: Methanol

Melting Point: 182.5 - 183.5°C

Form: Free

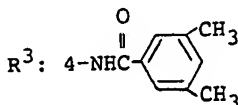
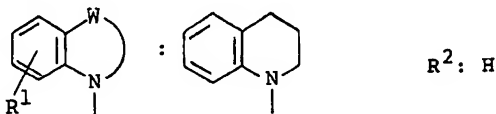
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Example 61

## Structure



Crystalline form: Colorless amorphous

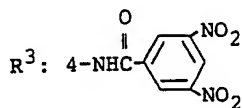
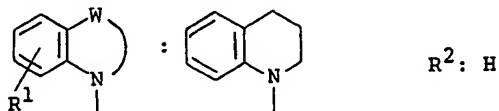
NMR analysis: 4)

Form: Free

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## Example 62

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 263 - 264°C

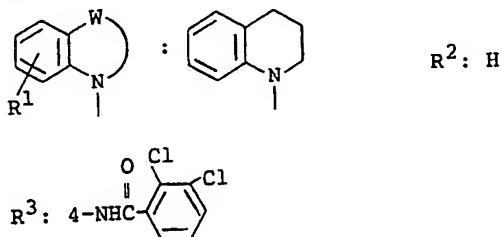
Form: Free

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Example 63

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

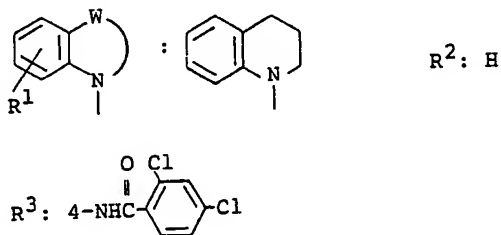
Melting Point: 217 - 218°C

Form: Free

---

## Example 64

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 183 - 184°C

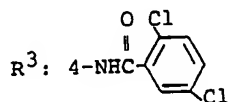
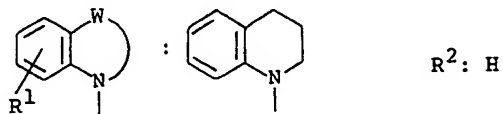
Form: Free

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Example 65

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Dichloromethane/ethanol

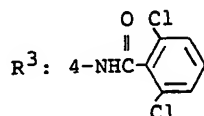
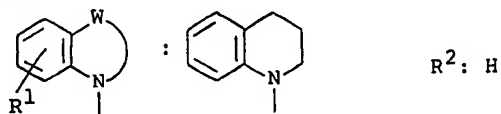
Melting Point: 207.5 - 208.5°C

Form: Free

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## Example 66

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 251 - 252°C

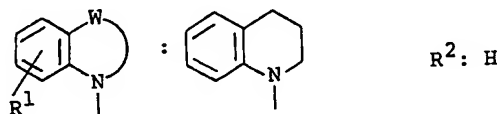
Form: Free

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---

Example 67

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

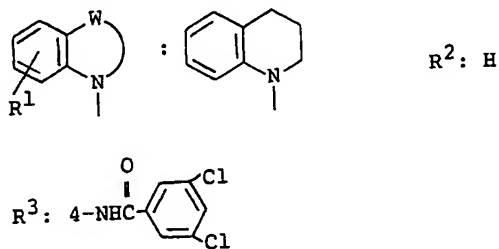
Melting Point: 208.5 - 209.5°C

Form: Free

---

## Example 68

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 231 - 232°C

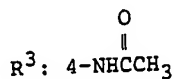
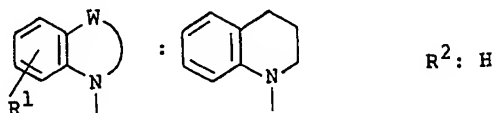
Form: Free

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Example 69

## Structure



Crystalline form: Colorless amorphous

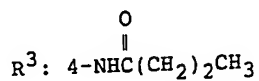
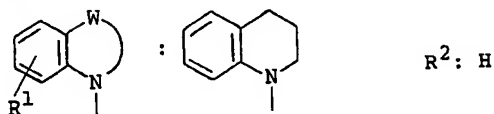
NMR analysis: 5)

Form: Free

---

## Example 70

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 134 - 135°C

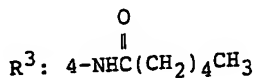
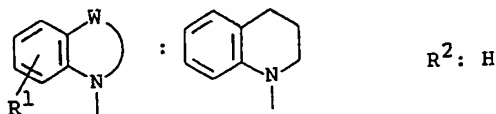
Form: Free

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Example 71

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

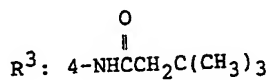
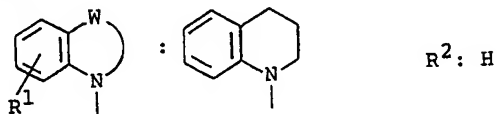
Melting Point: 115 - 116°C

Form: Free

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## Example 72

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 178.5 - 179.5°C

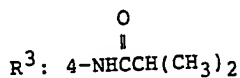
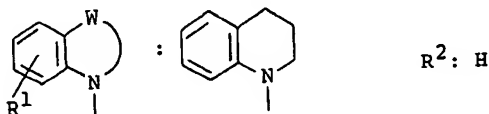
Form: Free

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Example 73

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

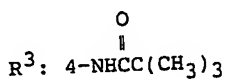
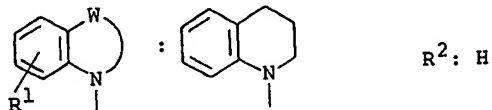
Melting Point: 182.5 - 183.5°C

Form: Free

---

## Example 74

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 164 - 165°C

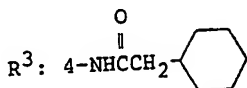
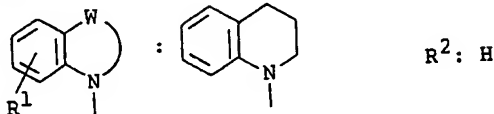
Form: Free

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Example 75

## Structure



Crystalline form: Colorless amorphous

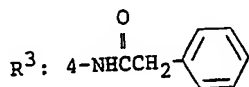
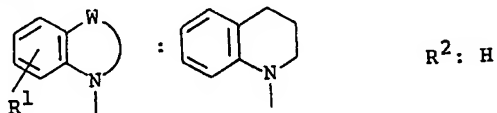
NMR analysis: 6)

Form: Free

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## Example 76

## Structure



Crystalline form: Yellow amorphous

NMR analysis: 7)

Form: Free

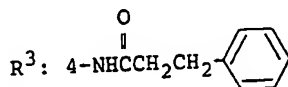
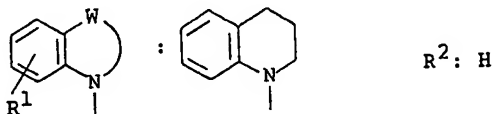
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Example 77

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

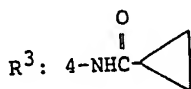
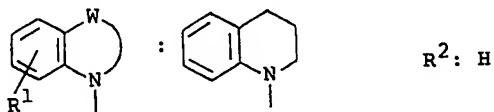
Melting Point: 155 - 156°C

Form: Free

---

## Example 78

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 182.5 - 183.5°C

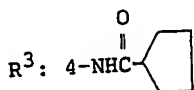
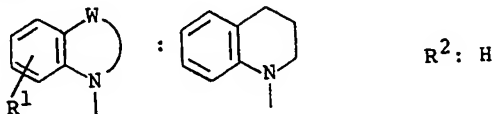
Form: Free

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Example 79

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

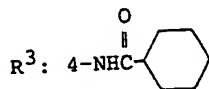
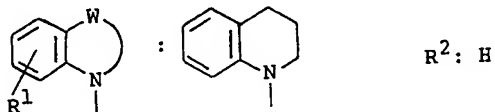
Melting Point: 164.5 - 165.5°C

Form: Free

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## Example 80

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 165 - 167°C

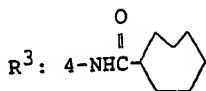
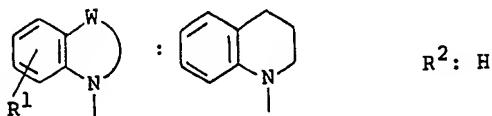
Form: Free

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Example 81

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

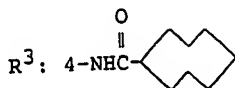
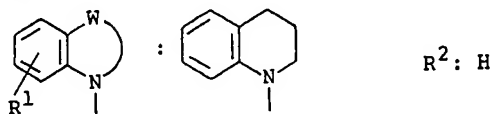
Melting Point: 124 - 125°C

Form: Free

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## Example 82

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 140.5 - 141.5°C

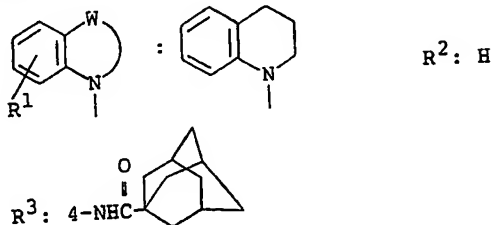
Form: Free

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Example 83

## Structure



Crystalline form: Colorless amorphous

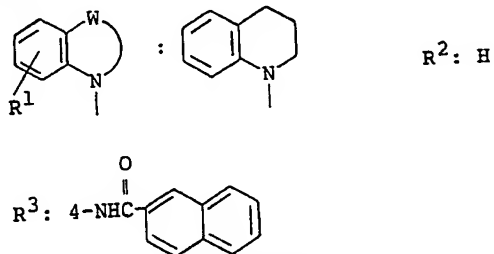
NMR analysis: 8)

Form: Free

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## Example 84

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 211 - 212°C

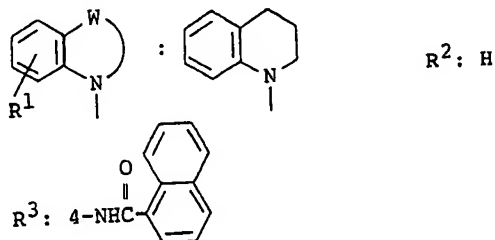
Form: Free

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Example 85

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

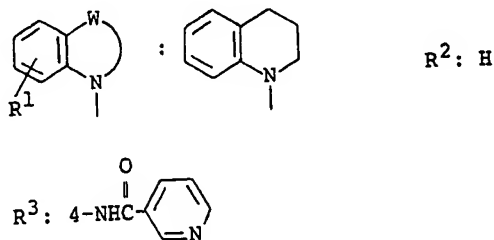
Melting Point: 178 - 179°C

Form: Free

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## Example 86

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 212.5 - 213.5°C

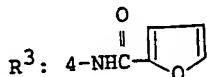
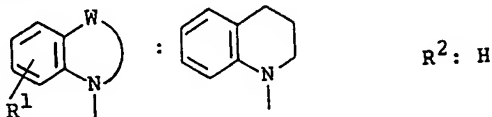
Form: Free

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Example 87

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

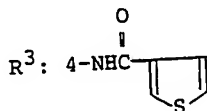
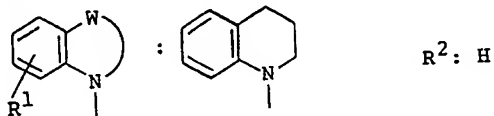
Melting Point: 193 - 194°C

Form: Free

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## Example 88

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 203 - 204°C

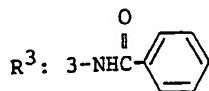
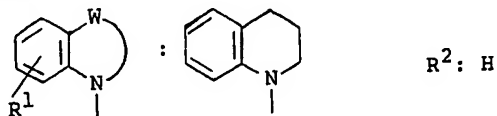
Form: Free

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Example 89

## Structure



Crystalline form: Colorless amorphous

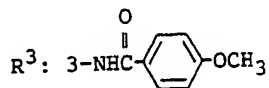
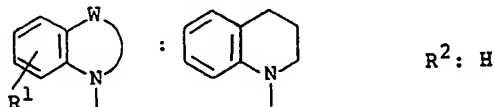
NMR analysis: 9)

Form: Free

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## Example 90

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 10)

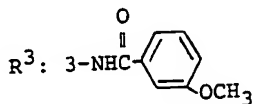
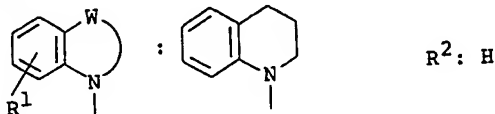
Form: Free

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Example 91

## Structure



Crystalline form: Colorless amorphous

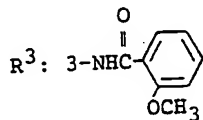
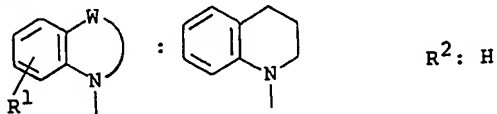
NMR analysis: 11)

Form: Free

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## Example 92

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 156.5 - 157.5°C

Form: Free

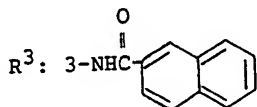
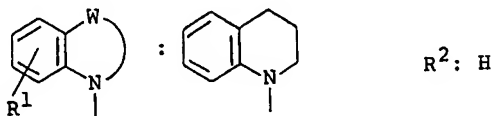
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Example 93

## Structure



Crystalline form: Colorless amorphous

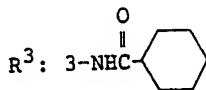
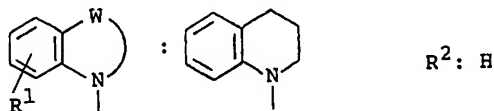
NMR analysis: 12)

Form: Free

---

## Example 94

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 203.5 - 204.5°C

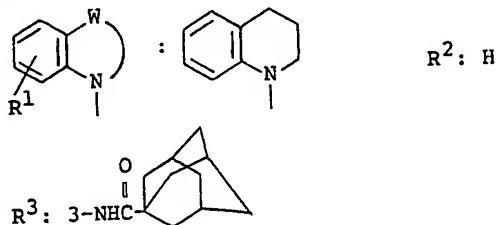
Form: Free

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Example 95

## Structure



Crystalline form: Colorless amorphous

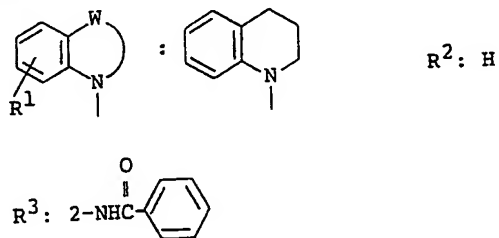
NMR analysis: 13)

Form: Free

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## Example 96

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

Melting Point: 126 - 127°C

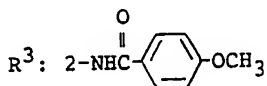
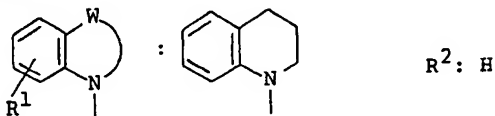
Form: Free

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Example 97

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

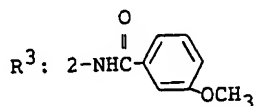
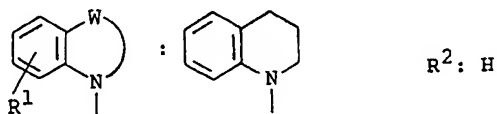
Melting Point: 158.5 - 159.5°C

Form: Free

---

## Example 98

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 129 - 130°C

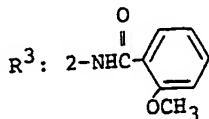
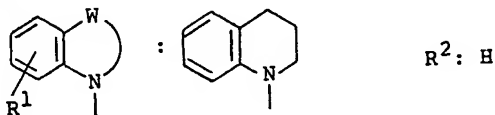
Form: Free

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Example 99

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

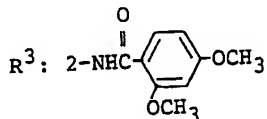
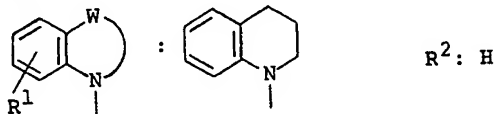
Melting Point: 131.5 - 132.5°C

Form: Free

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## Example 100

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 140 - 141°C

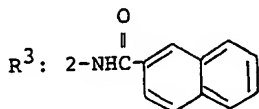
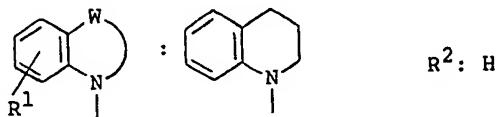
Form: Free

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Example 101

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

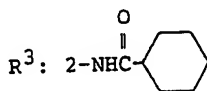
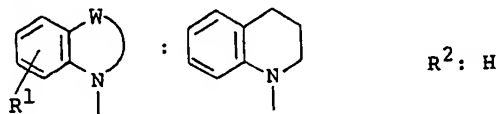
Melting Point: 138.5 - 139.5°C

Form: Free

---

## Example 102

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 128 - 129°C

Form: Free

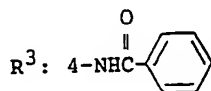
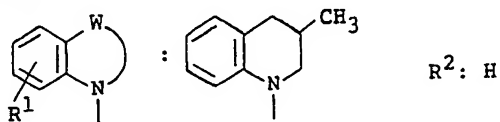
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Example 105

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

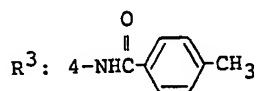
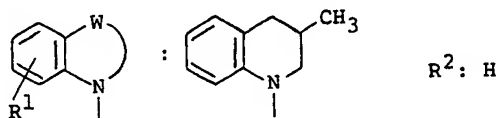
Melting Point: 197 - 198°C

Form: Free

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## Example 106

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 204 - 205°C

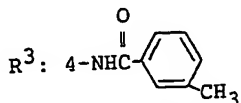
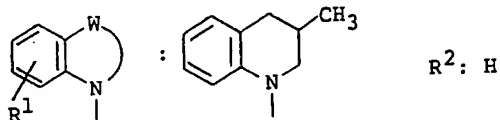
Form: Free

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Example 107

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

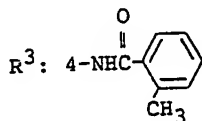
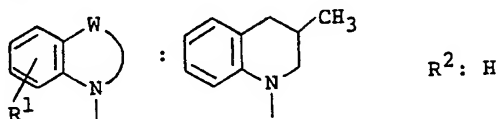
Melting Point: 174 - 175°C

Form: Free

---

## Example 108

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Methanol

Melting Point: 202 - 203°C

Form: Free

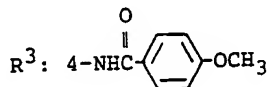
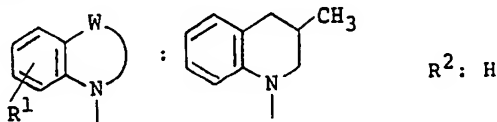
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Example 109

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

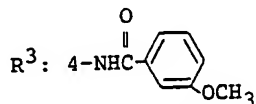
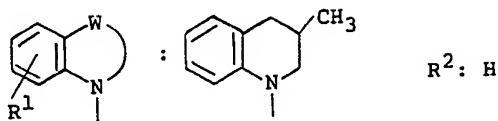
Melting Point: 203 - 204°C

Form: Free

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## Example 110

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 170.5 - 171.5°C

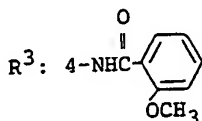
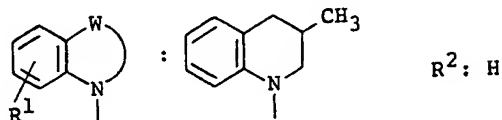
Form: Free

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Example 111

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

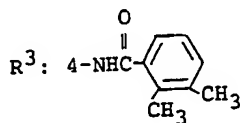
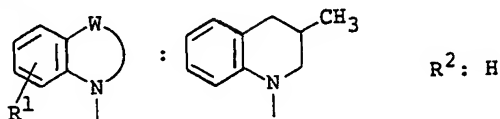
Melting Point: 149 - 150°C

Form: Free

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## Example 112

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 185 - 186°C

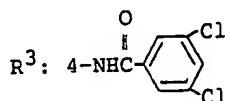
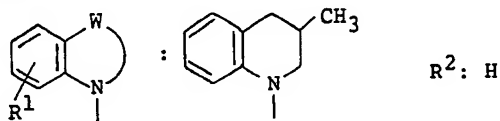
Form: Free

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Example 113

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

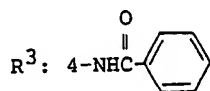
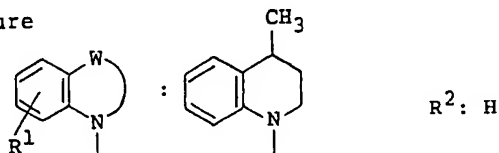
Melting Point: 225 - 226°C

Form: Free

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## Example 114

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 234 - 235°C

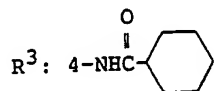
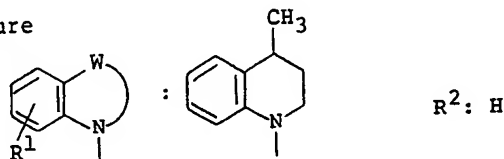
Form: Free

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Example 115

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

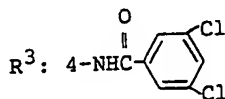
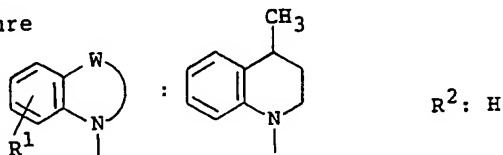
Melting Point: 149.5 - 150.5°C

Form: Free

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## Example 116

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

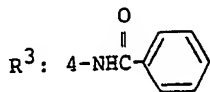
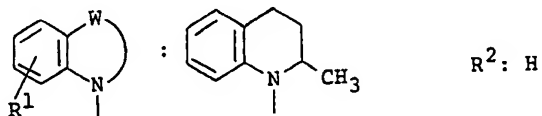
Melting Point: 197 - 198°C

Form: Free

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### Example 117

## Structure



Crystalline form: White powder

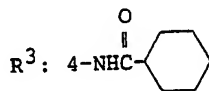
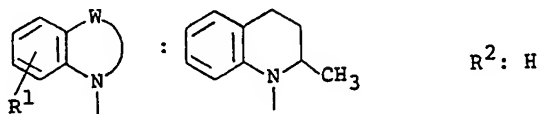
Recrystallization solvent: Methanol

Melting Point: 204 - 205°C

Form: Free

Example 118

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

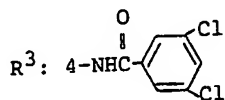
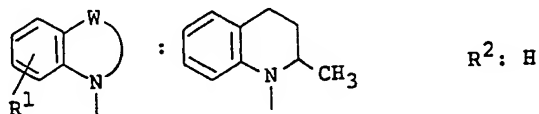
Melting Point: 224.5 - 225.5°C

Form: Free

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Example 119

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

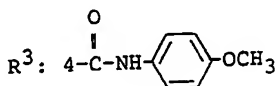
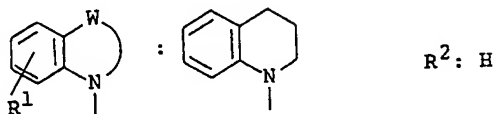
Melting Point: 189.5 - 190.5°C

Form: Free

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## Example 120

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 221.5 - 222.5°C

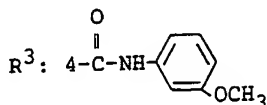
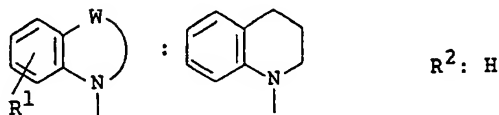
Form: Free

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Example 121

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Methanol

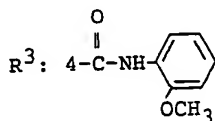
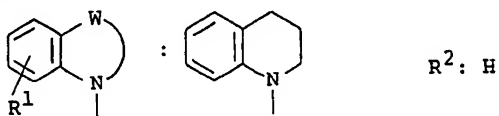
Melting Point: 154 - 155°C

Form: Free

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## Example 122

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 165 - 166°C

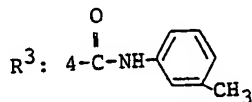
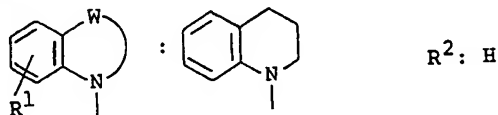
Form: Free

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Example 123

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Methanol

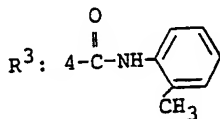
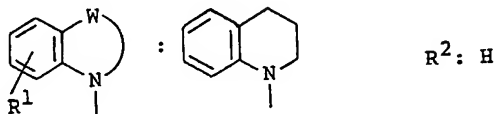
Melting Point: 141 - 142°C

Form: Free

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## Example 124

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 165.5 - 166.5°C

Form: Free

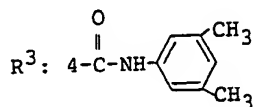
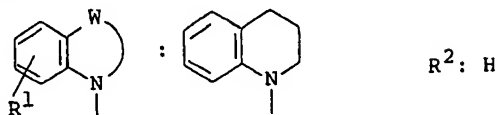
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Example 125

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Methanol

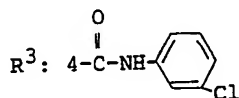
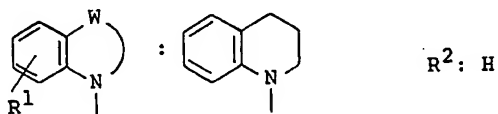
Melting Point: 164 - 165°C

Form: Free

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## Example 126

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 203.5 - 204.5°C

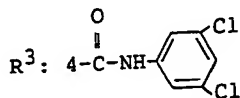
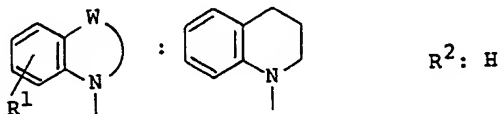
Form: Free

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Example 127

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

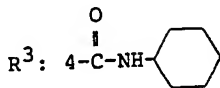
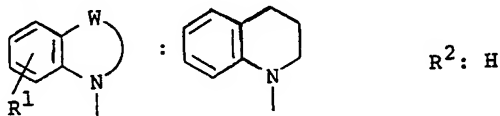
Melting Point: 236.5 - 237.5°C

Form: Free

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## Example 128

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 206.5 - 207.5°C

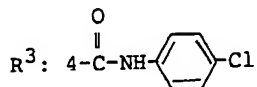
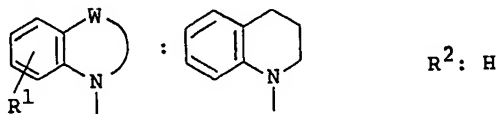
Form: Free

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Example 129

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

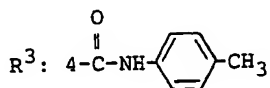
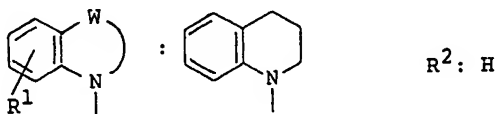
Melting Point: 271 - 272°C

Form: Free

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## Example 130

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 246 - 247°C

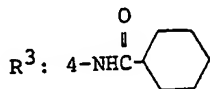
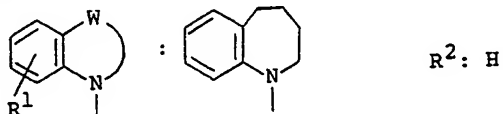
Form: Free

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Example 131

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

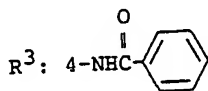
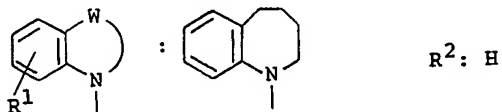
Melting Point: 210 - 211°C

Form: Free

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## Example 132

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 230.5 - 231.5°C

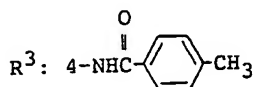
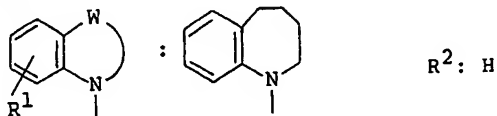
Form: Free

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Example 133

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

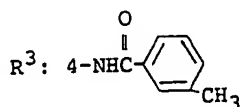
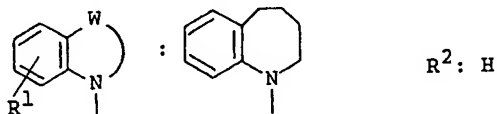
Melting Point: 203 - 204°C

Form: Free

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## Example 134

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 170 - 171°C

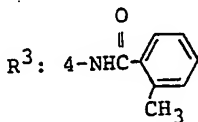
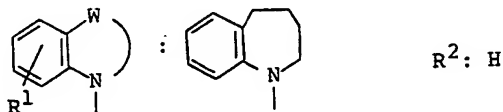
Form: Free

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Example 135

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

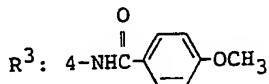
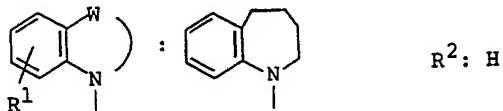
Melting Point: 225.5 - 226.5°C

Form: Free

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## Example 136

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 210.5 - 211.5°C

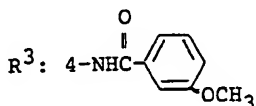
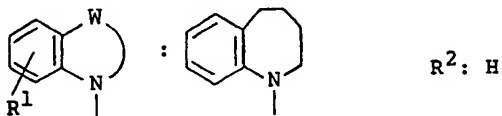
Form: Free

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Example 137

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

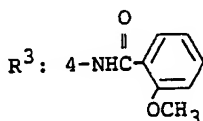
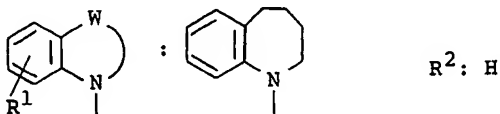
Melting Point: 183 - 184°C

Form: Free

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## Example 138

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 191.5 - 192.5°C

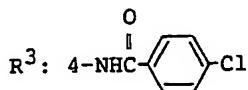
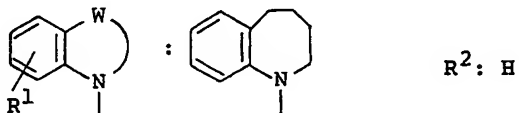
Form: Free

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Example 139

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

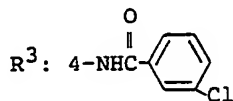
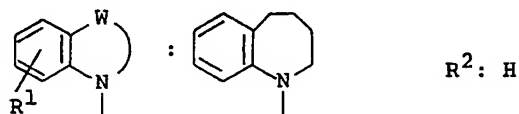
Melting Point: 203.5 - 204.5°C

Form: Free

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## Example 140

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 215.5 - 216.5°C

Form: Free

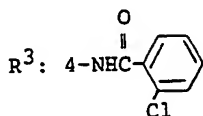
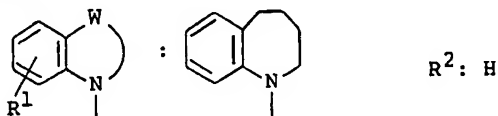
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Example 141

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

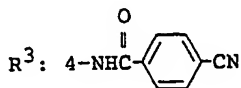
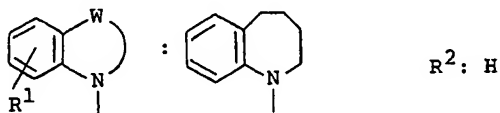
Melting Point: 211.5 - 212.5°C

Form: Free

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## Example 142

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 280.5 - 281.5°C

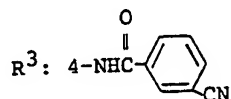
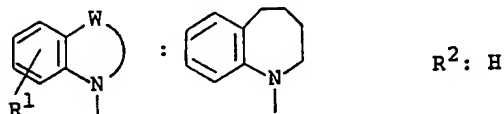
Form: Free

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Exempl 143

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

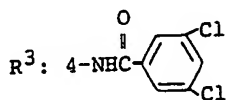
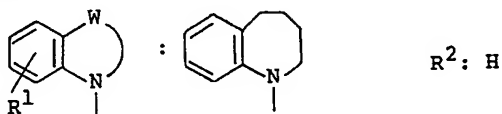
Melting Point: 235.5 - 236.5°C

Form: Free

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## Example 144

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/dichloromethane

Melting Point: 249.5 - 250.5°C

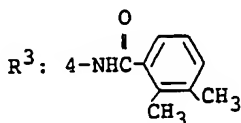
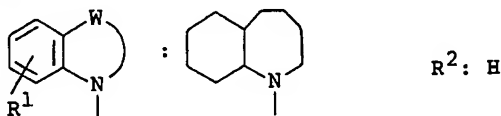
Form: Free

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Example 145

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

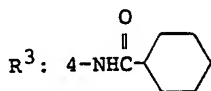
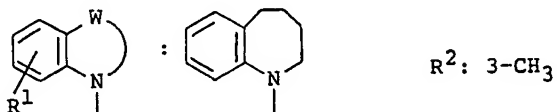
Melting Point: 217 - 218°C

Form: Free

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## Example 146

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 201.5 - 203°C

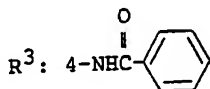
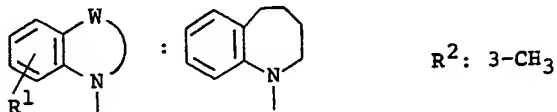
Form: Free

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Example 147

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

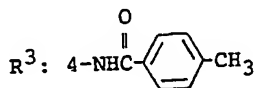
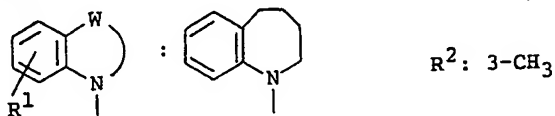
Melting Point: 221 - 222°C

Form: Free

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## Example 148

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 193 - 194°C

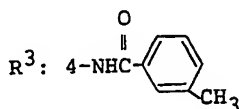
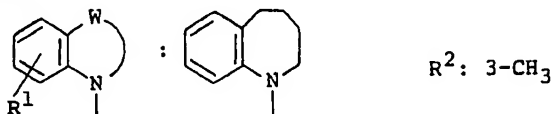
Form: Free

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Example 149

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

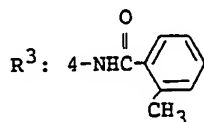
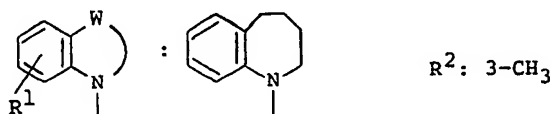
Melting Point: 176 - 177°C

Form: Free

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## Example 150

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 188 - 189.5°C

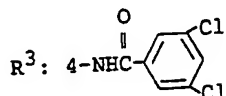
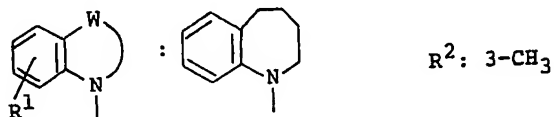
Form: Free

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Example 151

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

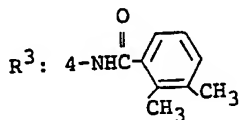
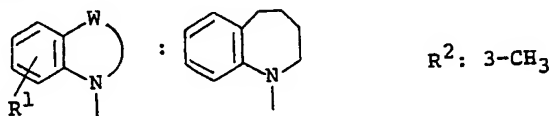
Melting Point: 227 - 228°C

Form: Free

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## Example 152

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 186 - 187°C

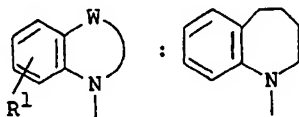
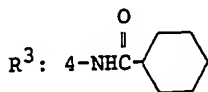
Form: Free

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Example 153

## Structure

 $R^2: 3\text{-OCH}_3$ 

Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

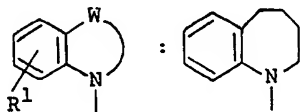
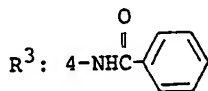
Melting Point: 135 - 136°C

Form: Free

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## Example 154

## Structure

 $R^2: 3\text{-OCH}_3$ 

Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 173 - 174°C

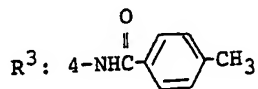
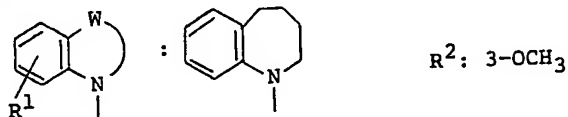
Form: Free

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Example 155

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

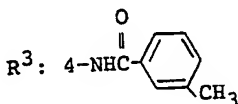
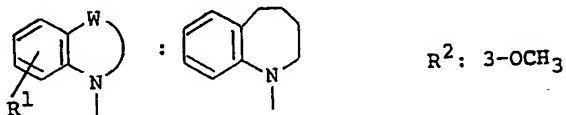
Melting Point: 174.5 - 175.5°C

Form: Free

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## Example 156

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 156 - 157°C

Form: Free

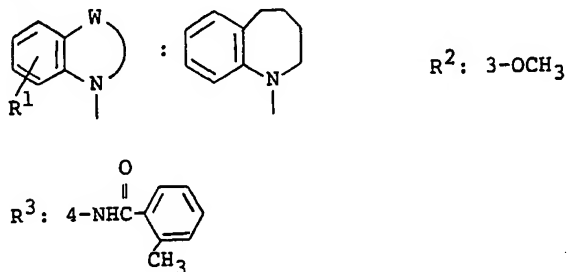
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Example 157

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

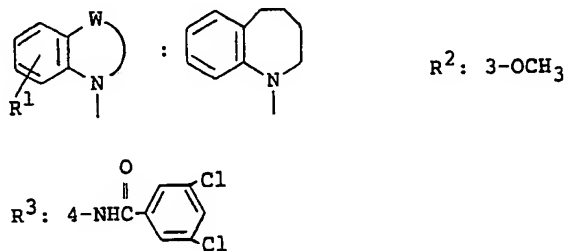
Melting Point: 153 - 154°C

Form: Free

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## Example 158

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 169 - 170°C

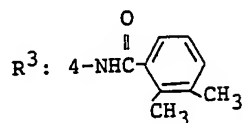
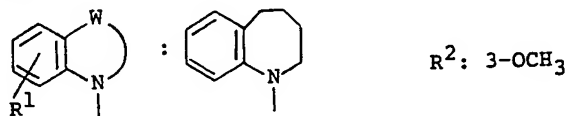
Form: Free

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Example 159

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

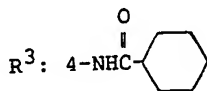
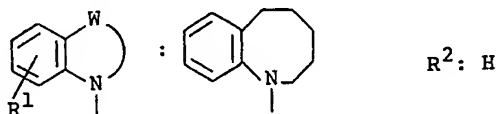
Melting Point: 185 - 186°C

Form: Free

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## Example 160

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 213 - 214°C

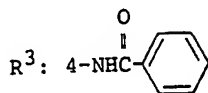
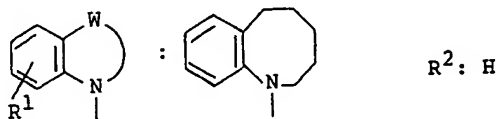
Form: Free

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Example 161

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

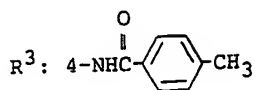
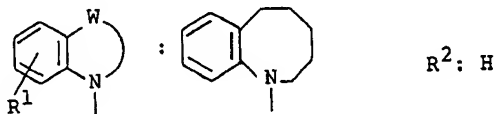
Melting Point: 240 - 241°C

Form: Free

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## Example 162

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 225 - 226°C

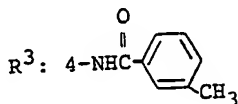
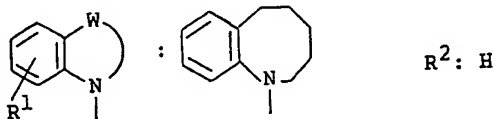
Form: Free

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Example 163

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

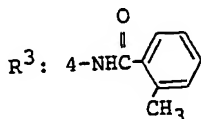
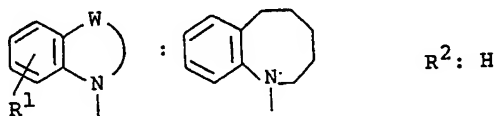
Melting Point: 209.5 - 210.5°C

Form: Free

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## Example 164

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 198 - 199°C

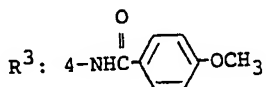
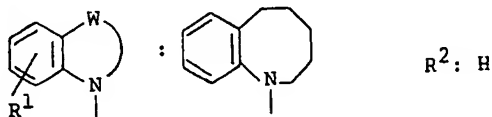
Form: Free

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Example 165

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

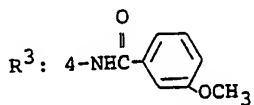
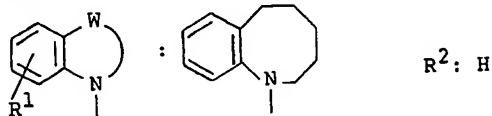
Melting Point: 214.5 - 215.5°C

Form: Free

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## Example 166

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

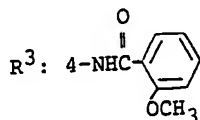
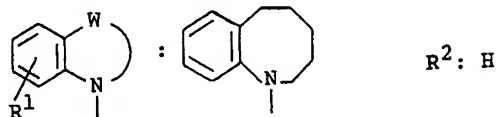
Melting Point: 196.5 - 197.5°C

Form: Free

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## Example 167

## Structure



Crystalline form: White powder

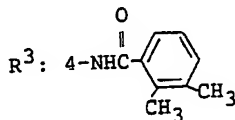
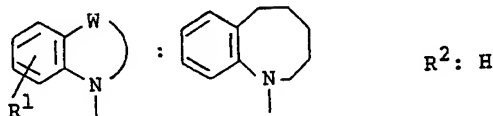
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 194 - 195°C

Form: Free

## Example 168

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

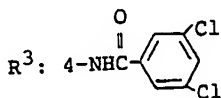
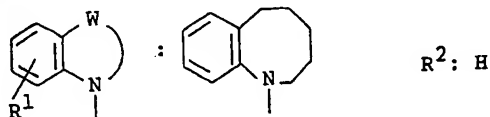
Melting Point: 191 - 192°C

Form: Free

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Example 169

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

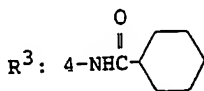
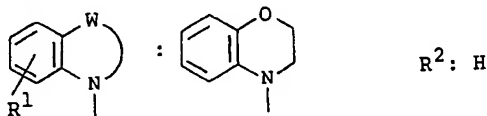
Melting Point: 227 - 228°C

Form: Free

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## Example 170

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 182 - 183°C

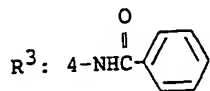
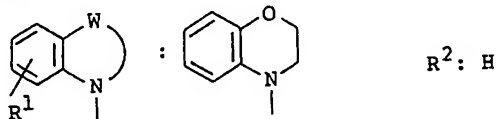
Form: Free

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Example 171

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

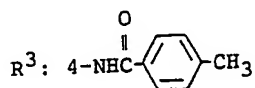
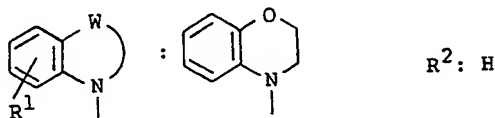
Melting Point: 222 - 223°C

Form: Free

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## Example 172

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 204 - 205°C

Form: Free

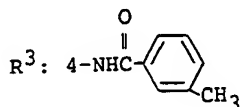
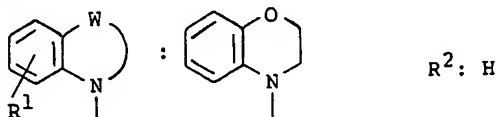
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Example 173

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

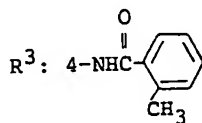
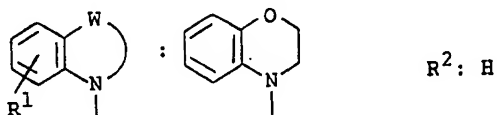
Melting Point: 194 - 195°C

Form: Free

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## Example 174

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 213 - 214°C

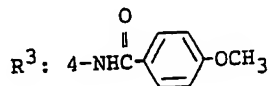
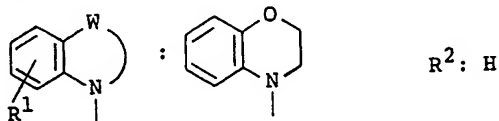
Form: Free

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Example 175

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

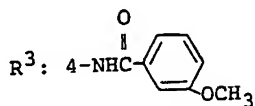
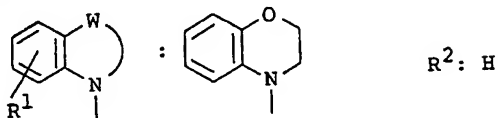
Melting Point: 201 - 202°C

Form: Free

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## Example 176

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 173 - 174°C

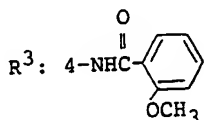
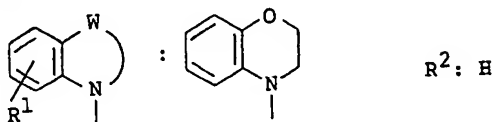
Form: Free

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Example 177

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

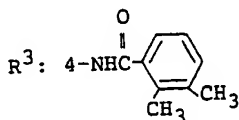
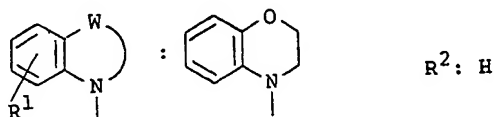
Melting Point: 150.5 - 151.5°C

Form: Free

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## Example 178

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 207.5 - 208.5°C

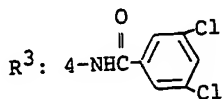
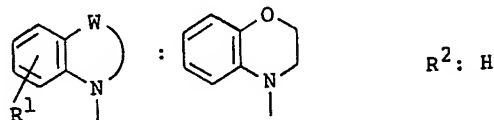
Form: Free

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Example 179

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

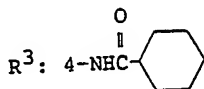
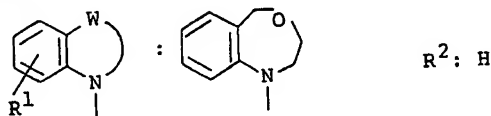
Melting Point: 256.5 - 257.5°C

Form: Free

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## Example 180

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 199.5 - 200.5°C

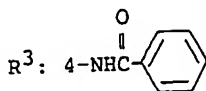
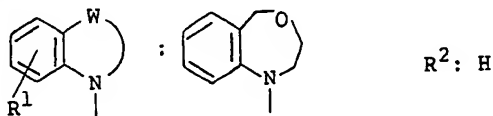
Form: Free

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Example 181

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

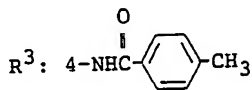
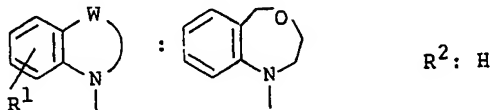
Melting Point: 211 - 212°C

Form: Free

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## Example 182

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 189.5 - 190.5°C

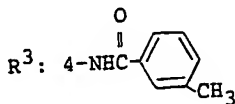
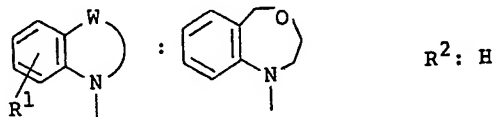
Form: Free

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Example 183

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

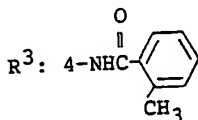
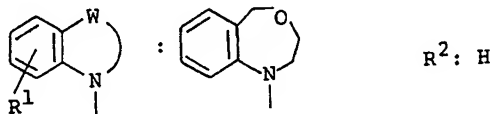
Melting Point: 176.5 - 177.5°C

Form: Free

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## Example 184

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 202 - 203°C

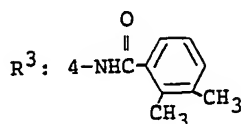
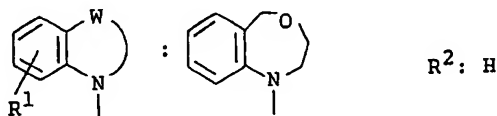
Form: Free

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Example 185

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

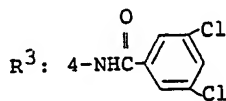
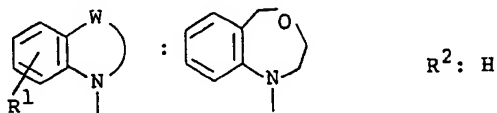
Melting Point: 219 - 220°C

Form: Free

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## Example 186

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 272 - 273°C

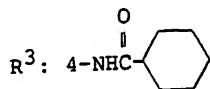
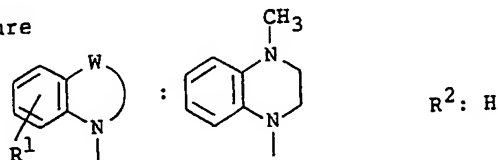
Form: Free

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Example 187

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

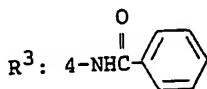
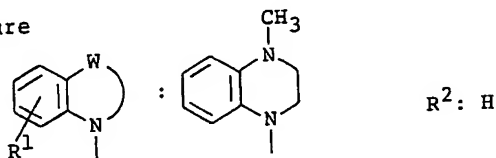
Melting Point: 146 - 147°C

Form: Free

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## Example 188

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 229.5 - 230.5°C

Form: Free

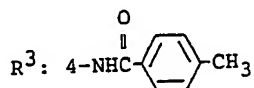
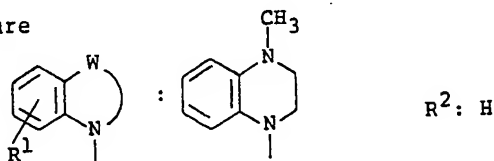
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Example 189

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

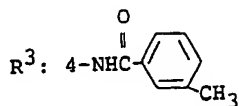
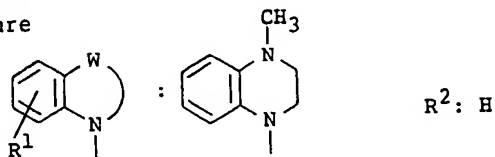
Melting Point: 119.5 - 120.5°C

Form: Free

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## Example 190

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 189 - 190°C

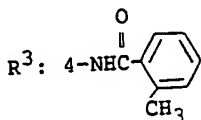
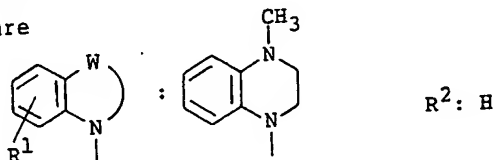
Form: Free

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Example 191

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

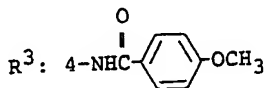
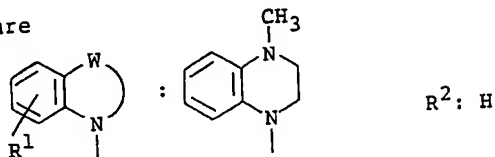
Melting Point: 207 - 208°C

Form: Free

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## Example 192

## Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 196.5 - 197.5°C

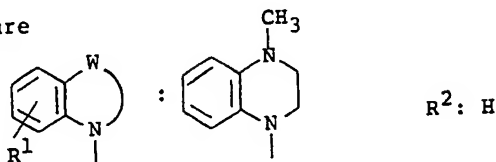
Form: Free

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Example 193

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

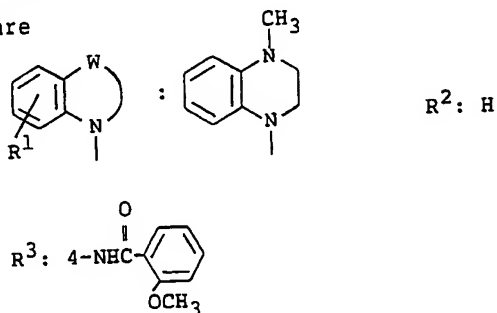
Melting Point: 182 - 183°C

Form: Free

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## Example 194

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 172 - 173°C

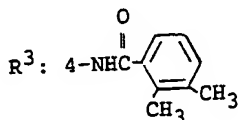
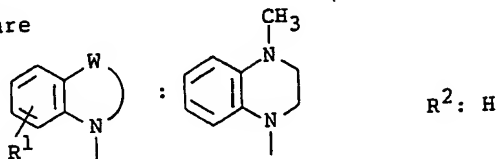
Form: Free

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Example 195

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

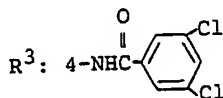
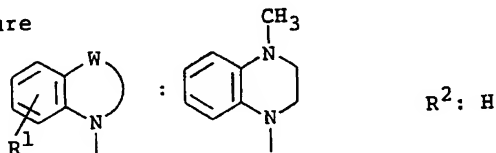
Melting Point: 197.5 - 198.5°C

Form: Free

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## Example 196

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 227 - 228°C

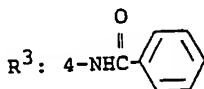
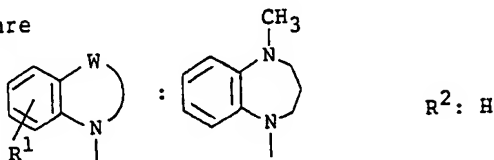
Form: Free

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Example 197

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

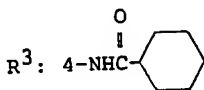
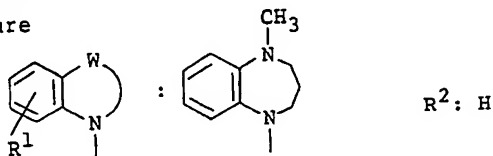
Melting Point: 216.5 - 217.5°C

Form: Free

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## Example 198

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 207 - 208°C

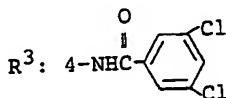
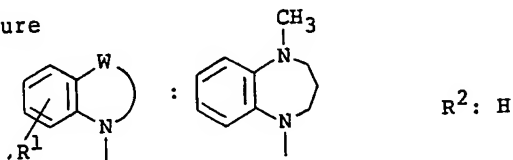
Form: Free

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Example 199

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

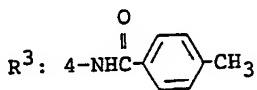
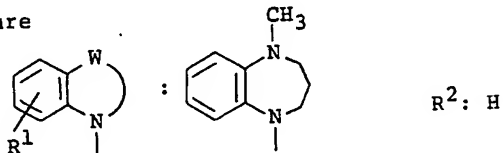
Melting Point: 236 - 237°C

Form: Free

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## Example 200

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 199.5 - 200.5°C

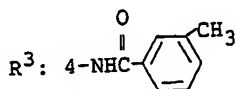
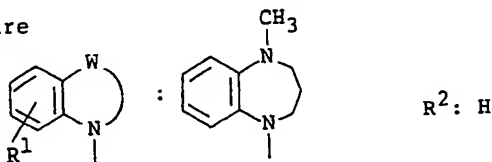
Form: Free

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Example 201

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

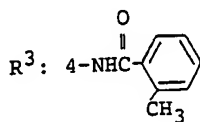
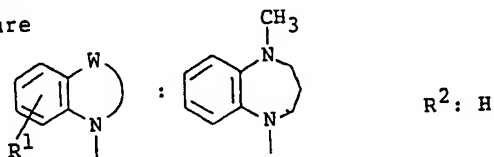
Melting Point: 171.5 - 172.5°C

Form: Free

---

## Example 202

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 222.5 - 223.5°C

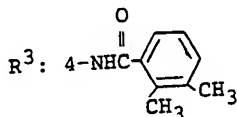
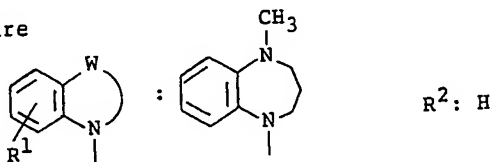
Form: Free

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Example 203

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

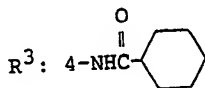
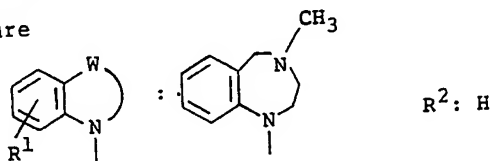
Melting Point: 209.5 - 210.5°C

Form: Free

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## Example 204

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

NMR analysis: 14)

Form: Hydrochloride

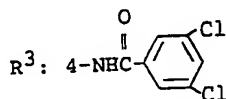
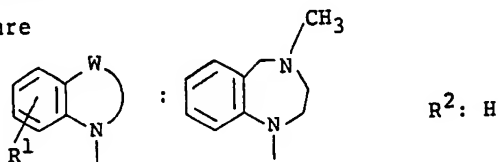
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Example 205

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

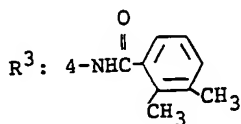
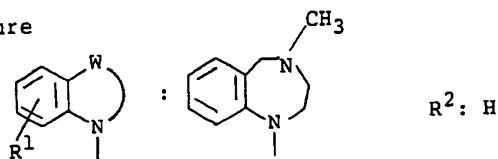
NMR analysis: 15)

Form: Hydrochloride

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## Example 206

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

NMR analysis: 16)

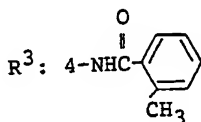
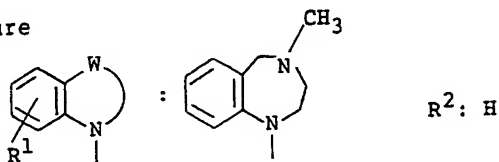
Form: Hydrochloride

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Example 207

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

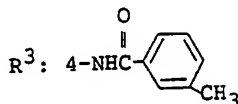
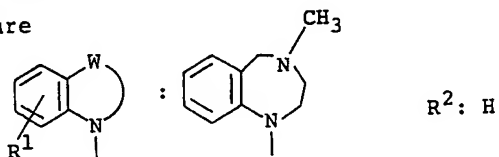
NMR analysis: 17)

Form: Hydrochloride

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## Example 208

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

NMR analysis: 18)

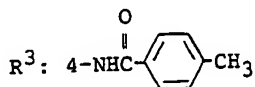
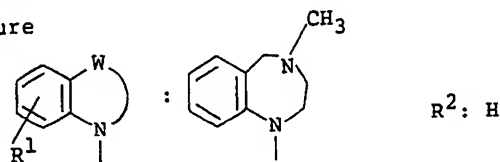
Form: Hydrochloride

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Example 209

Structure



Crystalline form: Yellow powder

Recrystallization solvent: Ethanol/water

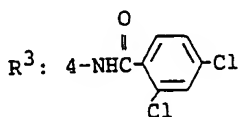
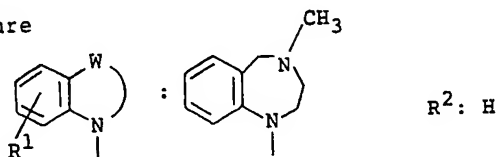
NMR analysis: 19)

Form: Hydrochloride

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## Example 210

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

NMR analysis: 20)

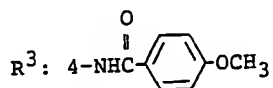
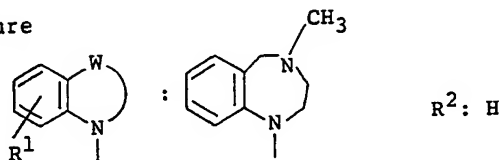
Form: Hydrochloride

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Example 211

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

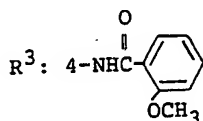
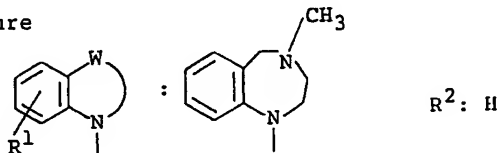
Melting Point: 159.5 - 160.5°C

Form: Free

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## Example 212

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 189.5 - 190.5°C

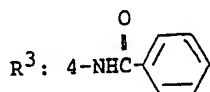
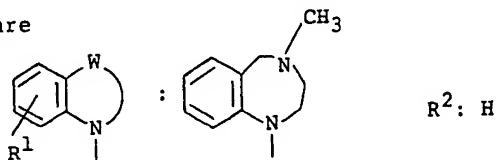
Form: Free.

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Example 213

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

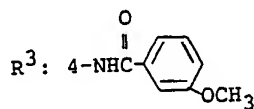
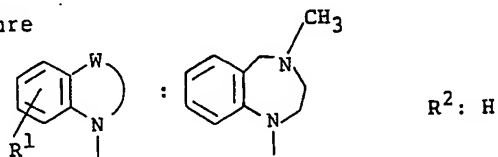
Melting Point: 170.5 - 171.5°C

Form: Free

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## Example 214

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

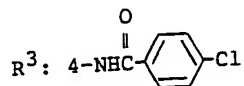
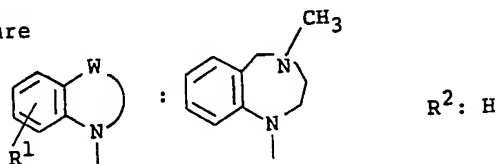
Melting Point: 165 - 166°C

Form: Free

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## Example 215

Structure



Crystalline form: White powder

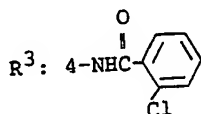
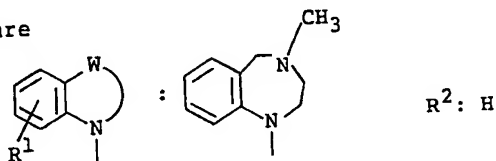
Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 173.5 - 174.5°C

Form: Free

## Example 216

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

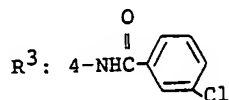
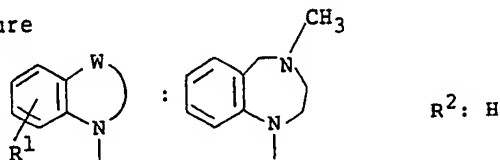
Melting Point: 182 - 183°C

Form: Free

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Example 217

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

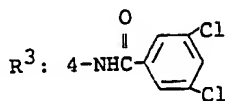
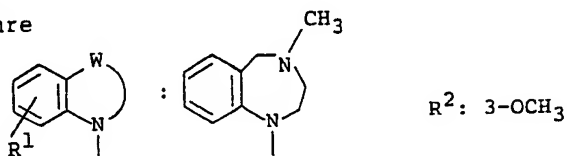
Melting Point: 225.5 - 226.5°C

Form: Free

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## Example 219

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

NMR analysis: 21)

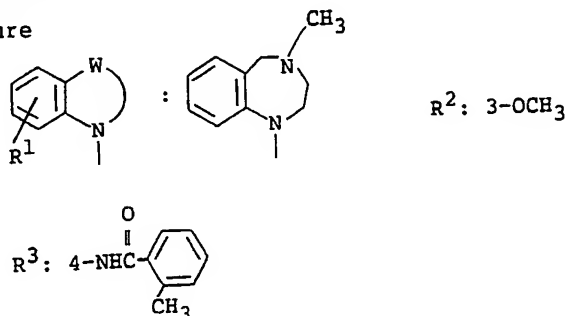
Form: Hydrochloride

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Example 220

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

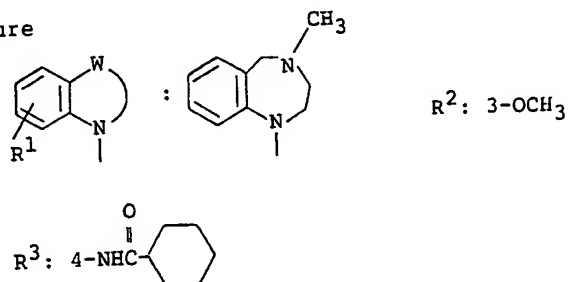
Melting Point: 147.5 - 148.5°C

Form: Free

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## Example 221

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 136 - 137°C

Form: Free

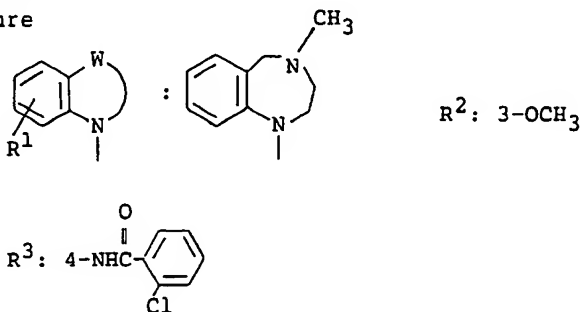
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Example 222

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

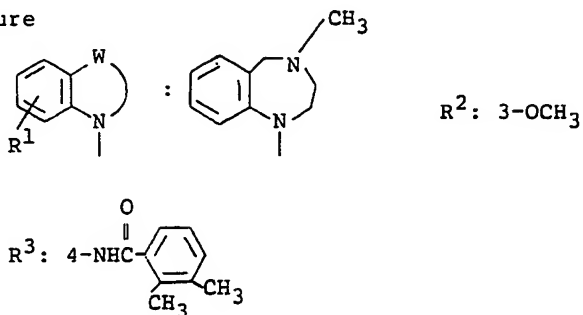
Melting Point: 191.5 - 192.5°C

Form: Free

---

## Example 223

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

Melting Point: 145 - 146°C

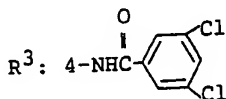
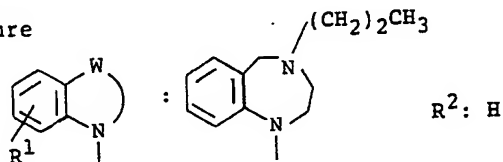
Form: Free

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Example 224

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

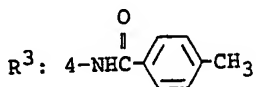
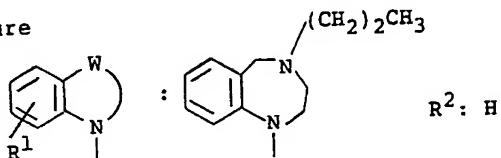
NMR analysis: 22)

Form: Hydrochloride

---

## Example 225

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

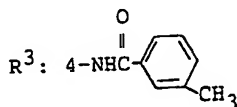
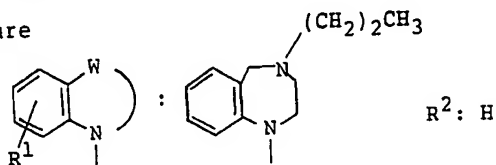
NMR analysis: 23)

Form: Hydrochloride

---

## Example 226

Structure



Crystalline form: White powder

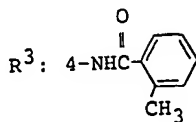
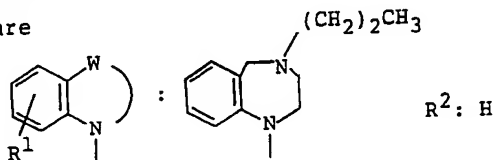
Recrystallization solvent: Ethanol/water

NMR analysis: 24)

Form: Hydrochloride

## Example 227

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

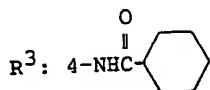
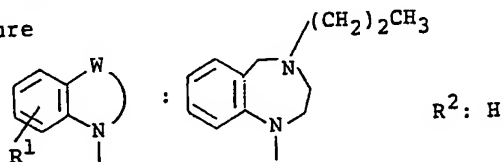
NMR analysis: 25)

Form: Hydrochloride

---

Example 228

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

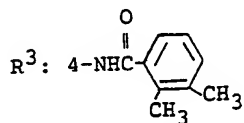
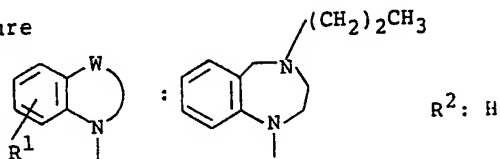
NMR analysis: 26)

Form: Hydrochloride

---

## Example 229

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

NMR analysis: 27)

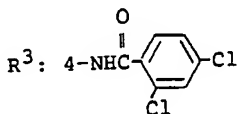
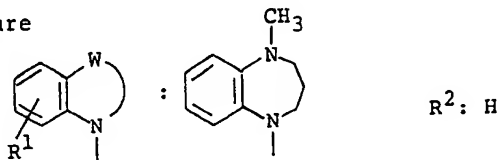
Form: Hydrochloride

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Example 230

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/diethyl ether

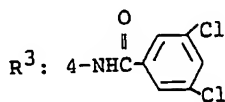
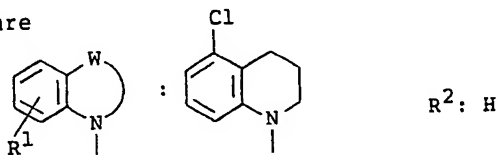
Melting Point: 206 - 207°C

Form: Free

---

## Example 231

## Structure



Crystalline form: White powder

Recrystallization solvent: Chloroform/methanol

Melting Point: 211 - 213°C

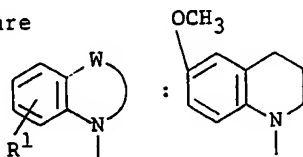
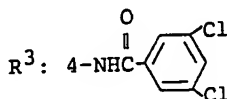
Form: Free

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Example 232

Structure

 $R^2: H$ 

Crystalline form: White powder

Recrystallization solvent: Chloroform/methanol

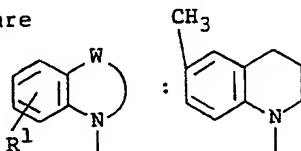
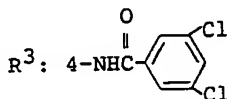
Melting Point: 228.5 - 229.5°C

Form: Free

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## Example 233

Structure

 $R^2: H$ 

Crystalline form: White powder

Recrystallization solvent: Chloroform/methanol

Melting Point: 237 - 238°C

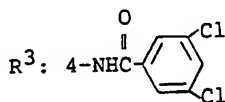
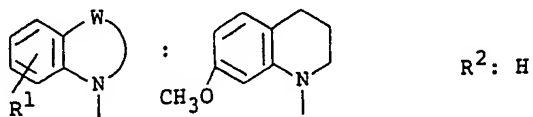
Form: Free

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Example 234

## Structure



Crystalline form: White powder

Recrystallization solvent: Chloroform/methanol

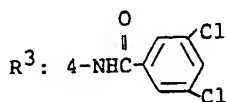
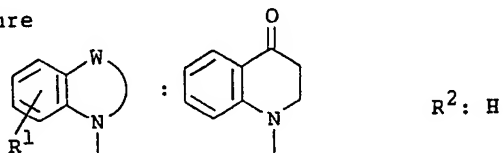
Melting Point: 226 - 228°C

Form: Free

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## Example 235

## Structure



Crystalline form: White powder

Recrystallization solvent: Chloroform/methanol

Melting Point: 220 - 222°C

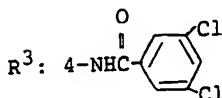
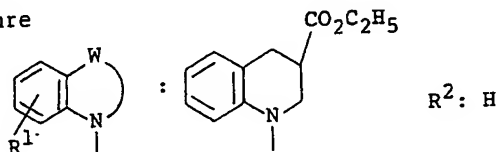
Form: Free

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Example 236

Structure



Crystalline form: Colorless amorphous

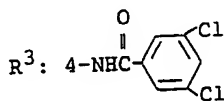
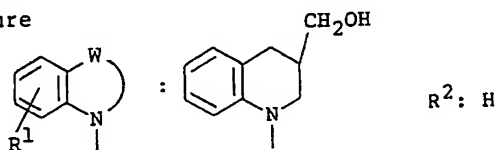
NMR analysis: 28)

Form: Free

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## Example 237

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 162 - 165°C

Form: Free

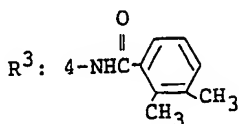
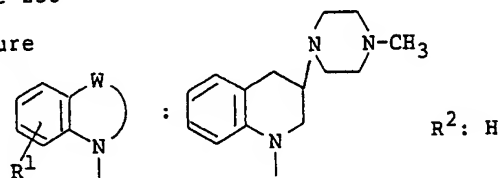
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Example 238

Structure



Crystalline form: Light brown amorphous

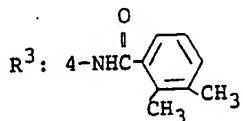
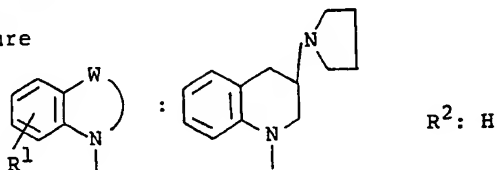
NMR analysis: 29)

Form: Free

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## Example 239

Structure



Crystalline form: Light brown amorphous

NMR analysis: 30)

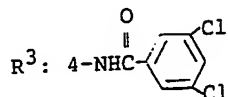
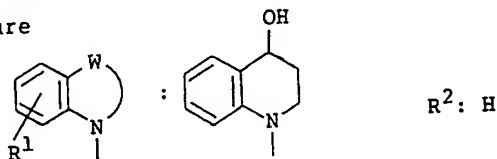
Form: Free

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Example 240

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

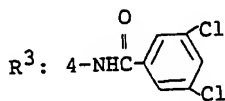
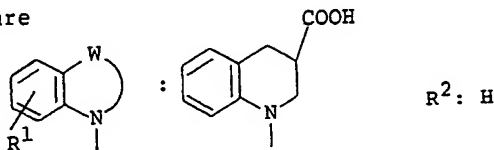
Melting Point: 215 - 217°C

Form: Free

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## Example 241

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 221 - 223°C

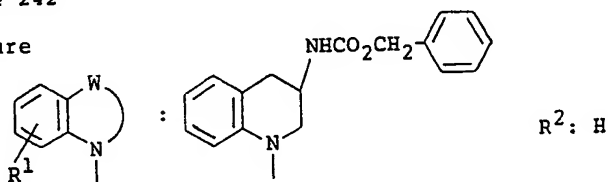
Form: Free

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Example 242

Structure



Crystalline form: Colorless amorphous

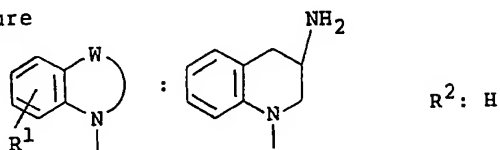
NMR analysis: 31)

Form: Free

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## Example 243

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 207 - 210°C

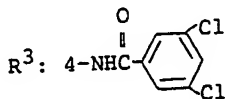
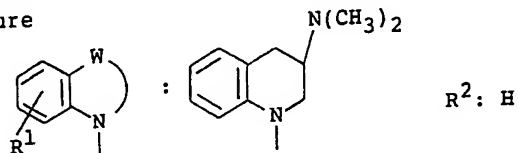
Form: Free

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Example 244

Structure



Crystalline form: Colorless amorphous

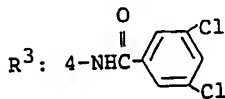
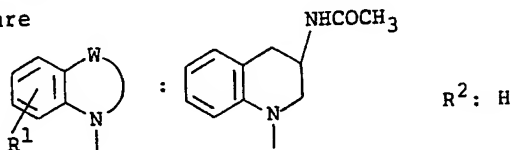
NMR analysis: 32)

Form: Free

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## Example 245

Structure



Crystalline form: Colorless amorphous

NMR analysis: 33)

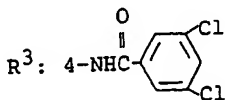
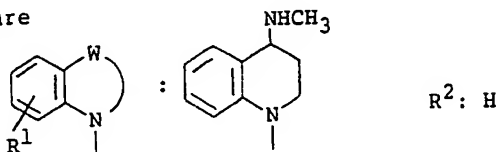
Form: Free

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Example 246

Structure



Crystalline form: Colorless amorphous

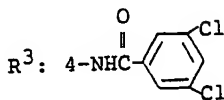
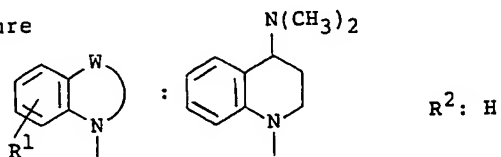
NMR analysis: 34)

Form: Free

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## Example 247

Structure



Crystalline form: Colorless amorphous

NMR analysis: 35)

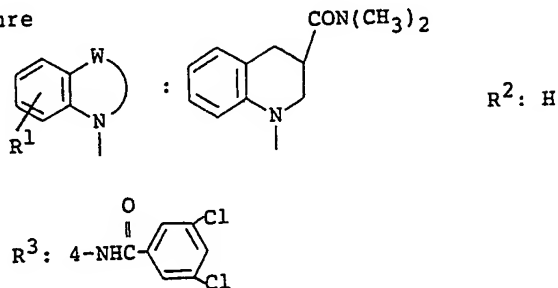
Form: Free

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Example 248

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Ethanol

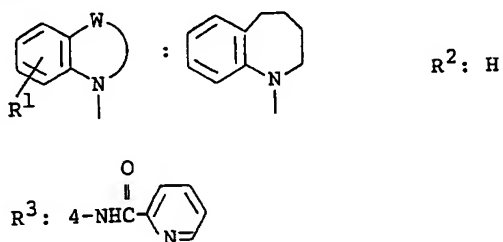
Melting Point: 186 - 187°C

Form: Free

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## Example 249

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

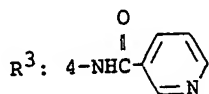
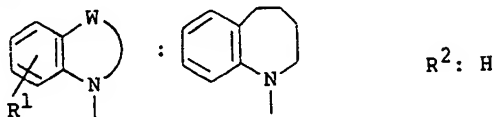
Melting Point: 190 - 191°C

Form: Free

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### Example 250

## Structure



Crystalline form: Light yellow scales

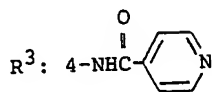
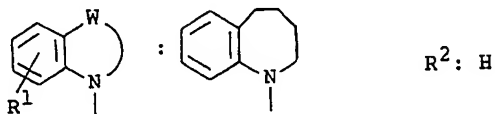
Recrystallization solvent: Ethanol/water

Melting Point: 230 - 231°C

Form: Free

Example 251

## Structure



Crystalline form: Light yellow needles

Recrystallization solvent: Ethanol

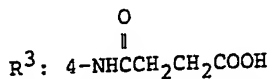
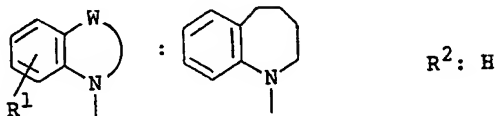
Melting Point: 227 - 228°C

Form: Free

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Example 252

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethyl acetate

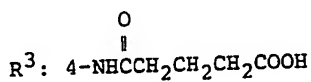
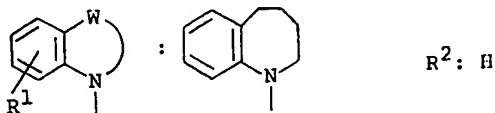
Melting Point: 192°C

Form: Free

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## Example 253

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 186.5 - 189°C

Form: Free

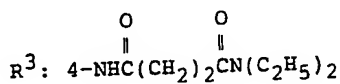
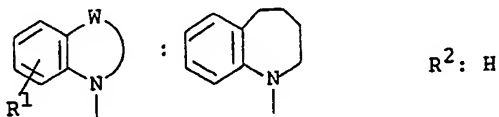
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Example 254

## Structure



Crystalline form: Light yellow scales

Recrystallization solvent: n-Hexane/ethyl acetate

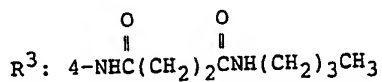
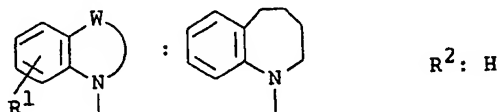
Melting Point: 165 - 167°C

Form: Free

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## Example 255

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 169 - 170°C

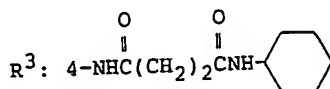
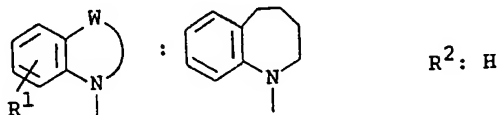
Form: Free

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Example 256

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: n-Hexane/ethyl acetate

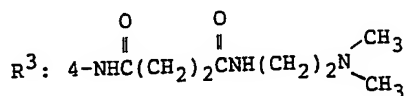
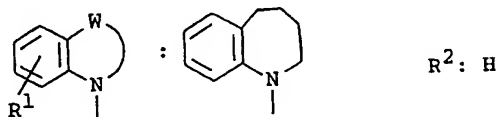
Melting Point: 174 - 177°C

Form: Free

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## Example 257

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 114 - 118°C

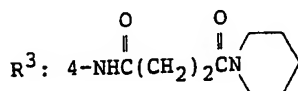
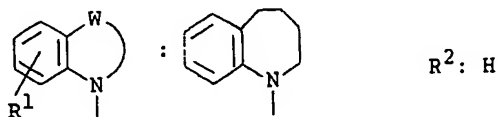
Form: Free

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Example 258

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

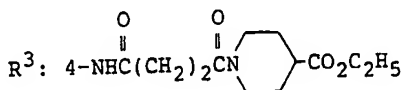
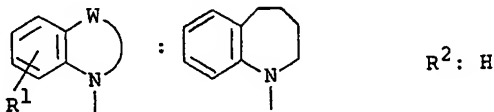
Melting Point: 170 - 172°C

Form: Free

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## Example 259

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 179 - 181°C

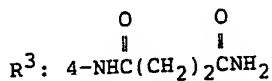
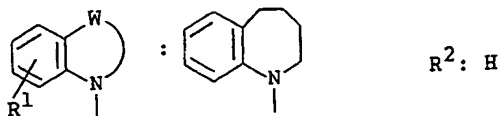
Form: Free

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Example 260

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

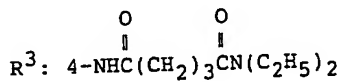
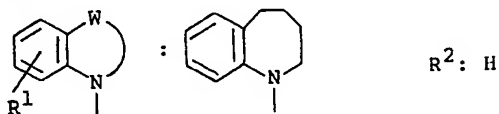
Melting Point: 118 - 121°C

Form: Free

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## Example 261

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 144 - 148°C

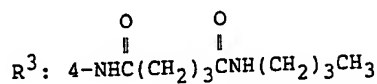
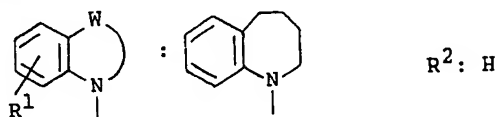
Form: Free

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Example 262

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: Ethyl acetate

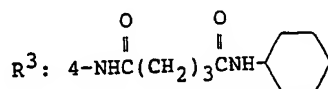
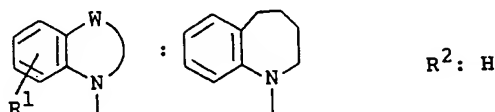
Melting Point: 156 - 157°C

Form: Free

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## Example 263

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 204 - 206°C

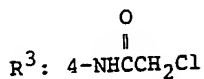
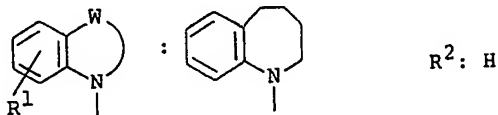
Form: Free

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Example 264

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: n-Hexane/ethyl acetate

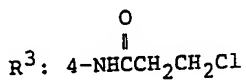
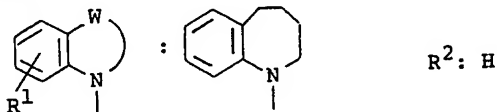
Melting Point: 165 - 167°C

Form: Free

---

## Example 265

## Structure



Crystalline form: Light yellow amorphous

NMR analysis: 36)

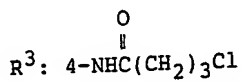
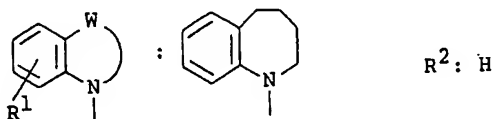
Form: Free

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Example 266

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

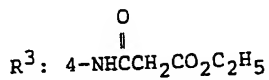
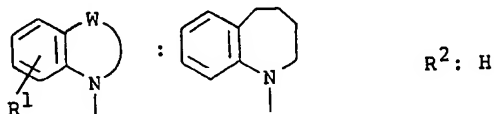
Melting Point: 122 - 124°C

Form: Free

---

## Example 267

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 116 - 117°C

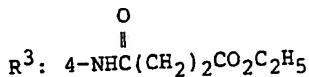
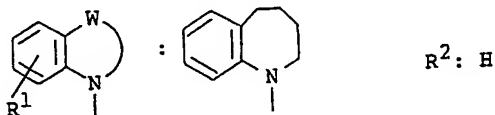
Form: Free

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Example 268

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

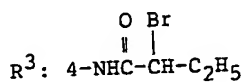
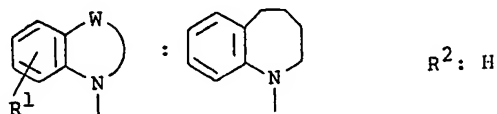
Melting Point: 121 - 123°C

Form: Free

---

## Example 269

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethyl acetate

Melting Point: 186 - 187°C

Form: Free

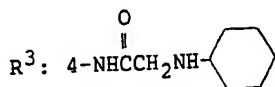
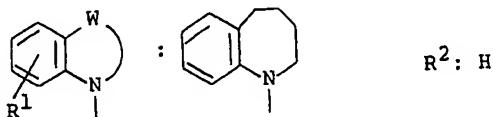
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Example 270

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

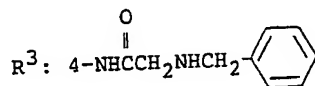
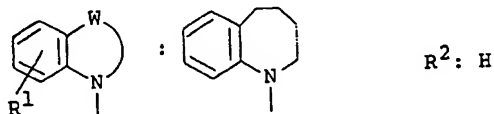
Melting Point: 139 - 142°C

Form: Free

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## Example 271

## Structure



Crystalline form: Light yellow amorphous

NMR analysis: 37)

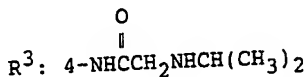
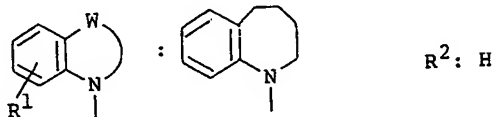
Form: Free

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Example 272

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

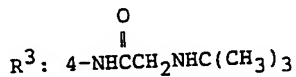
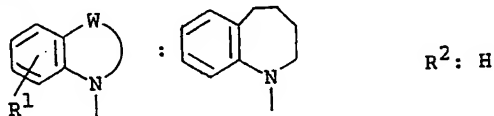
Melting Point: 149.5 - 152.5°C

Form: Free

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## Example 273

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

Melting Point: 150 - 152.5°C

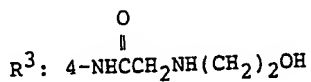
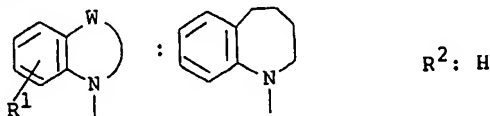
Form: Free

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Example 274

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

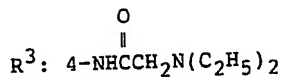
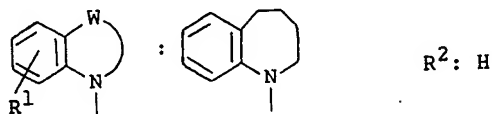
Melting Point: 150°C

Form: Free

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## Example 275

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 101 - 104°C

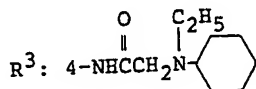
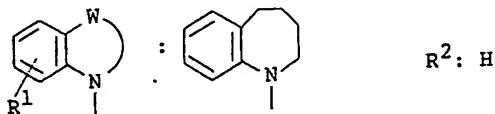
Form: Free

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Example 276

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

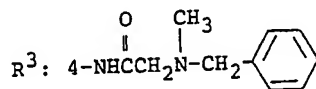
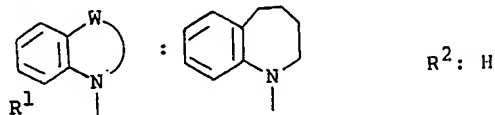
Melting Point: 120 - 122°C

Form: Free

---

## Example 277

## Structure



Crystalline form: Light yellow amorphous

NMR analysis: 38)

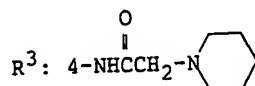
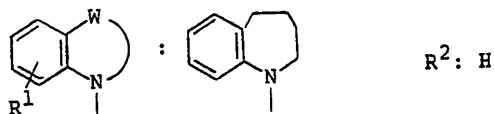
Form: Free

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Example 278

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

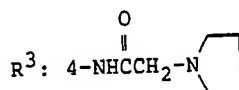
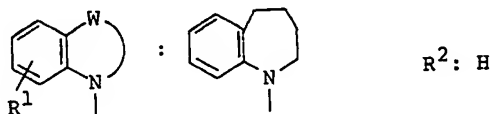
Melting Point: 183 - 186°C

Form: Free

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## Example 279

## Structure



Crystalline form: Light brown powder

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 139 - 142°C

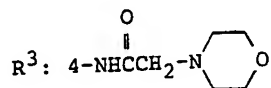
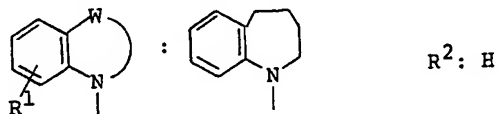
Form: Free

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Example 280

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Ethanol

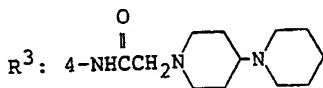
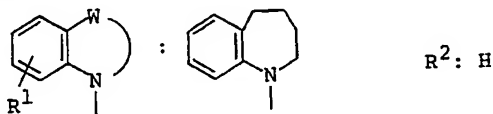
Melting Point: 162 - 165°C

Form: Free

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## Example 281

## Structure



Crystalline form: Light yellow scales

Recrystallization solvent: Ethyl acetate

Melting Point: 224 - 227°C

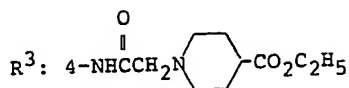
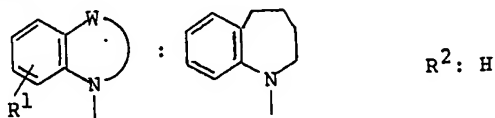
Form: Free

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Example 282

## Structure



Crystalline form: Light yellow amorphous

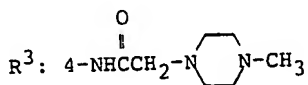
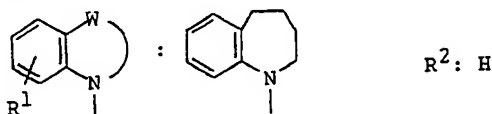
NMR analysis: 39)

Form: Free

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## Example 283

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Ethanol/water

Melting Point: 162 - 164°C

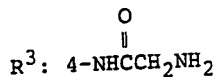
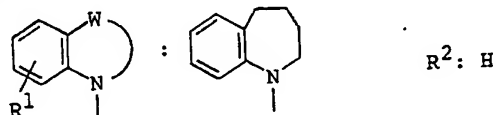
Form: Free

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Example 284

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Ethanol

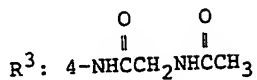
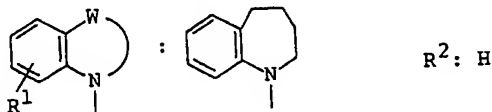
Melting Point: 238 - 241°C (decomposed)

Form: Hydrochloride

---

## Example 285

## Structure



Crystalline form: Light yellow amorphous

NMR analysis: 40)

Form: Free

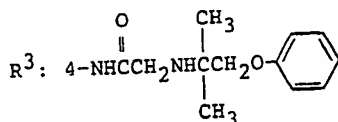
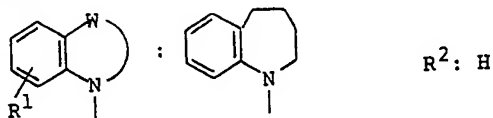
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Example 286

## Structure



Crystalline form: Colorless amorphous

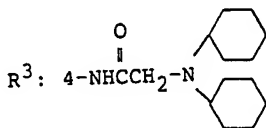
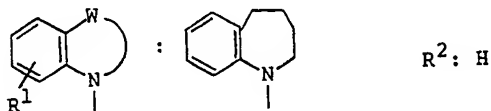
NMR analysis: 41)

Form: Free

---

## Example 287

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 168 - 169°C

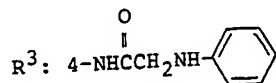
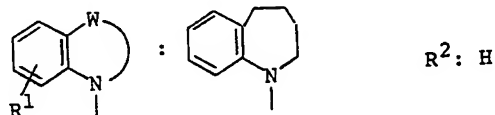
Form: Free

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Example 288

## Structure



Crystalline form: Light brown powder

Recrystallization solvent: Ethanol

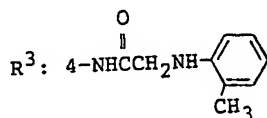
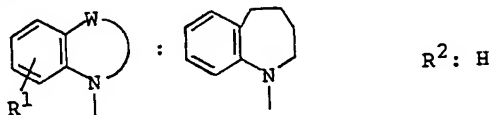
Melting Point: 189 - 191°C

Form: Free

---

## Example 289

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 200 - 202°C

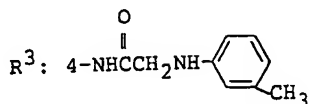
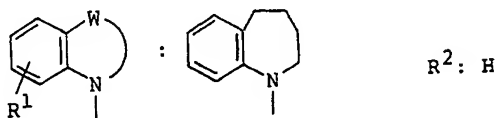
Form: Free

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Example 290

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: n-Hexane/ethyl acetate

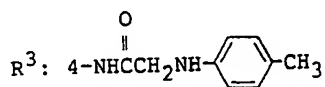
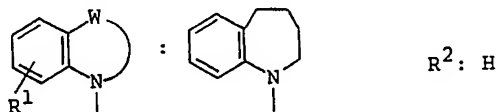
Melting Point: 143 - 146°C

Form: Free

---

## Example 291

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 117 - 117.5°C

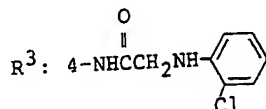
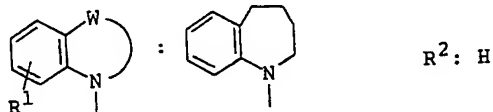
Form: Free

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Example 292

## Structure



Crystalline form: Light brown powder

Recrystallization solvent: Diethyl ether/ethyl acetate

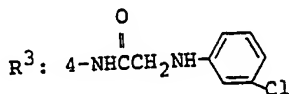
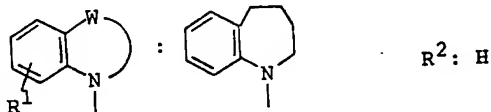
Melting Point: 225 - 226°C

Form: Free

---

## Example 293

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethanol

Melting Point: 175 - 176.5°C

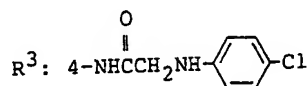
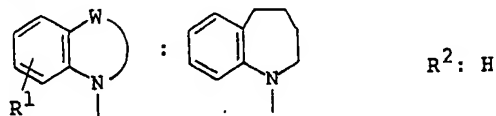
Form: Free

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Example 294

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

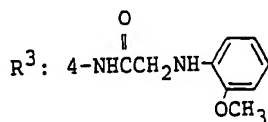
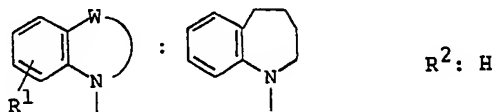
Melting Point: 234 - 236°C

Form: Free

---

## Example 295

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: Ethyl acetate

Melting Point: 172 - 174°C

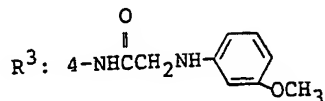
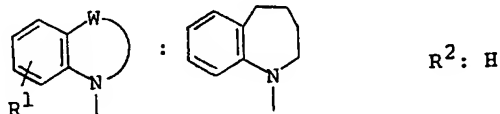
Form: Free

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Example 296

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

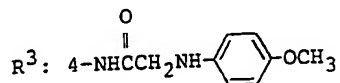
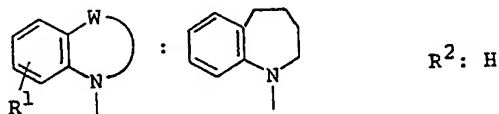
Melting Point: 154 - 155°C

Form: Free

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## Example 297

## Structure



Crystalline form: Light yellow needles

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 181.5 - 183.5°C

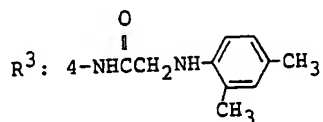
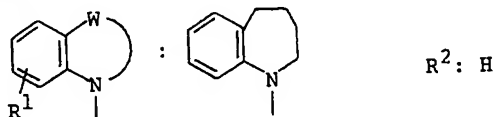
Form: Free

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Example 298

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

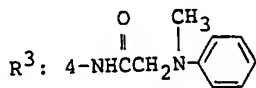
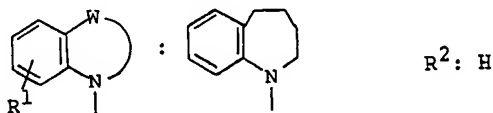
Melting Point: 173 - 175°C

Form: Free

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## Example 299

## Structure



Crystalline form: White powder

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 137 - 138°C

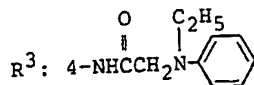
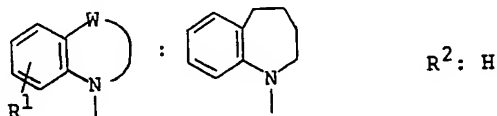
Form: Free

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Example 300

## Structure



Crystalline form: Light yellow amorphous

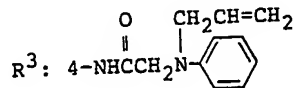
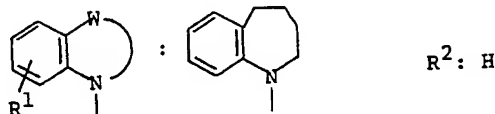
NMR analysis: 42)

Form: Free

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## Example 301

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Diethyl ether/ethyl acetate

Melting Point: 129 - 130°C

Form: Free

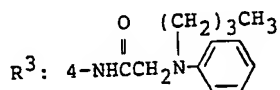
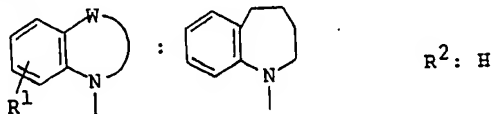
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Example 302

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: n-Hexane/ethyl acetate

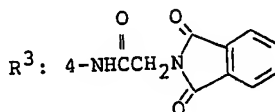
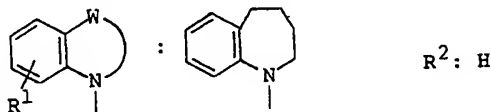
Melting Point: 181 - 183°C

Form: Free

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## Example 303

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 248 - 249°C

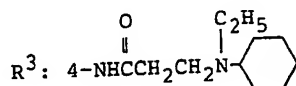
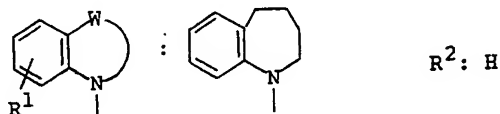
Form: Free

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Example 304

## Structure



Crystalline form: Light yellow amorphous . .

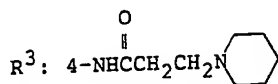
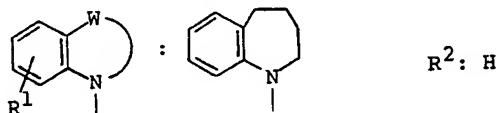
NMR analysis: 43)

Form: Free

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## Example 305

## Structure



Crystalline form: Light yellow needles

Recrystallization solvent: Ethanol

Melting Point: 94 - 96°C

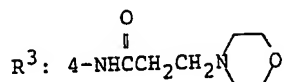
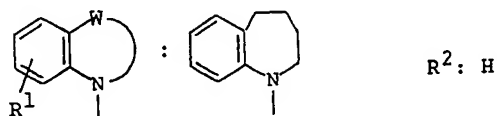
Form: Free

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Example 306

## Structure



Crystalline form: Light brown powder

Recrystallization solvent: Ethyl acetate

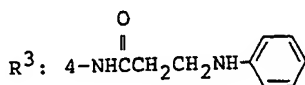
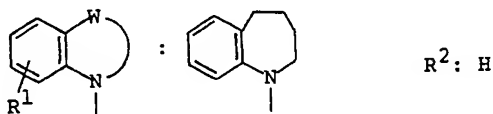
Melting Point: 159 - 161°C

Form: Free

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## Example 307

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 180 - 183°C

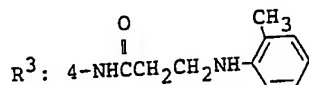
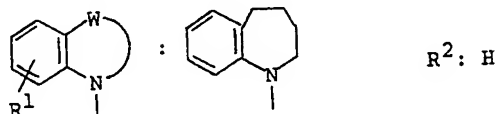
Form: Free

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Example 308

## Structure



Crystalline form: Light brown powder

Recrystallization solvent: Ethanol

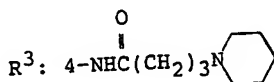
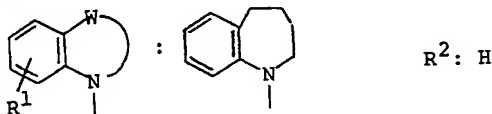
Melting Point: 177 - 180°C

Form: Free

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## Example 309

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 91 - 93°C

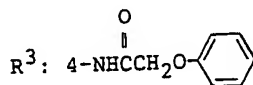
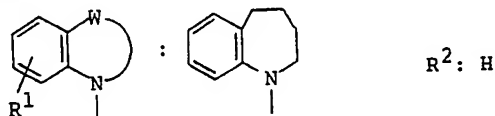
Form: Free

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Example 310

## Structure



Crystalline form: Light brown scales

Recrystallization solvent: Ethanol

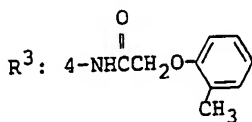
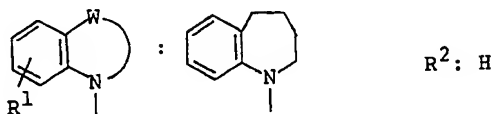
Melting Point: 155 - 156.5°C

Form: Free

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## Example 311

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: Ethyl acetate

Melting Point: 172.5 - 175°C

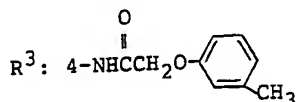
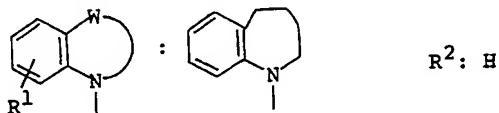
Form: Free

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Example 312

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

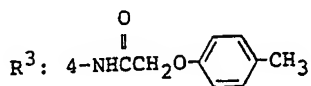
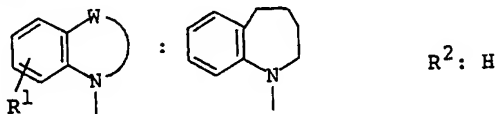
Melting Point: 148 - 150.5°C

Form: Free

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## Example 313

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 172 - 173°C

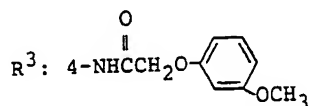
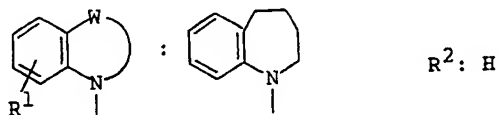
Form: Free

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Example 314

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: n-Hexane/ethyl acetate

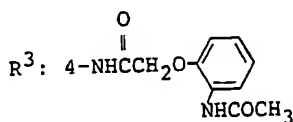
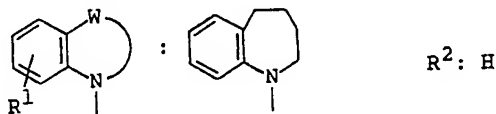
Melting Point: 133 - 135°C

Form: Free

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## Example 315

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 217 - 219°C

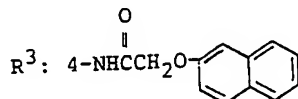
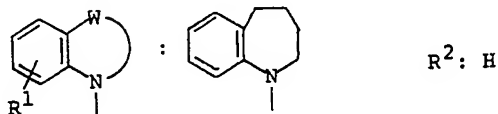
Form: Free

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Example 316

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethyl acetate

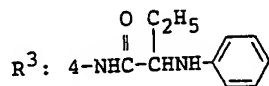
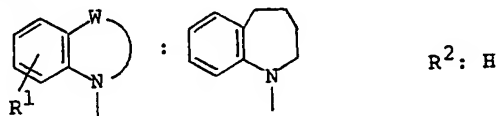
Melting Point: 226 - 227.5°C

Form: Free

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## Example 317

## Structure



Crystalline form: Colorless amorphous .

NMR analysis: 44)

Form: Free

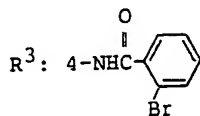
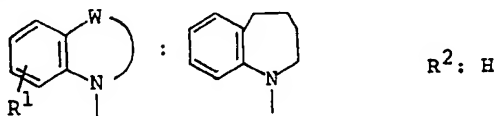
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Example 318

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane

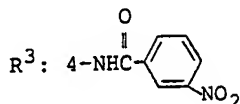
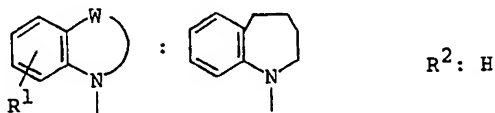
Melting Point: 234 - 235°C

Form: Free

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## Example 319

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Methanol

Melting Point: 218 - 218.5°C

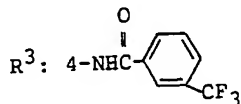
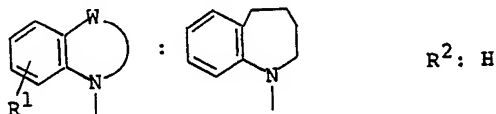
Form: Free

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Example 320

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

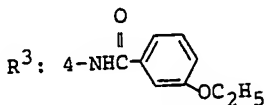
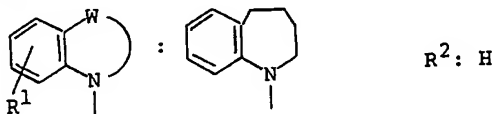
Melting Point: 202.5 - 206°C

Form: Free

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## Example 321

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 174 - 176°C

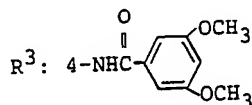
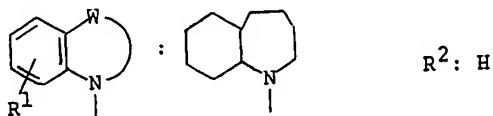
Form: Free

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Example 322

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

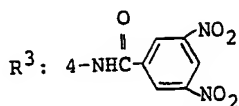
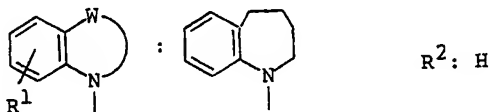
Melting Point: 216 - 218°C

Form: Free

---

## Example 323

## Structure



Crystalline form: White powder

Melting Point: &gt;300°C

NMR analysis: 45)

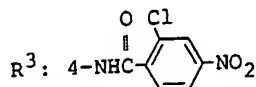
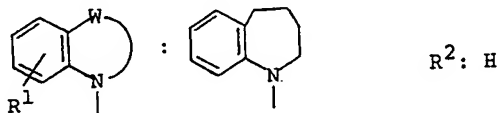
Form: Free

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Example 324

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

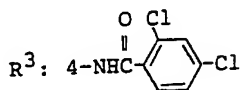
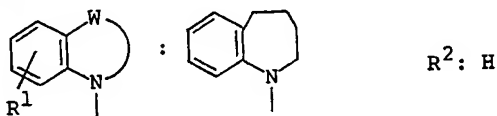
Melting Point: 250.5 - 251°C

Form: Free

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## Example 325

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

Melting Point: 223 - 225°C

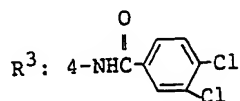
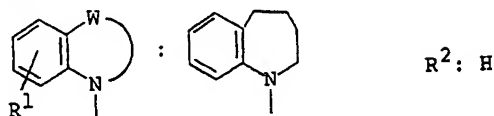
Form: Free

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Example 326

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Methanol

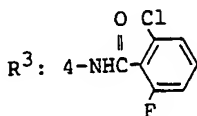
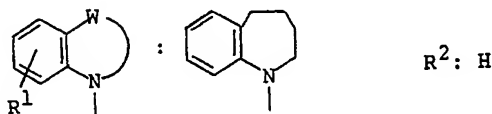
Melting Point: 213 - 214°C

Form: Free

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## Example 327

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

Melting Point: 246 - 247°C

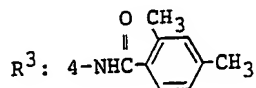
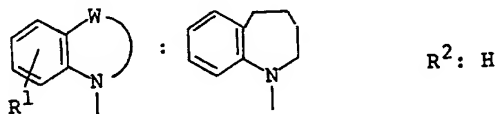
Form: Free

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Example 328

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Methanol

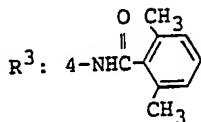
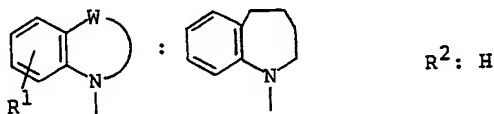
Melting Point: 248 - 251°C

Form: Free

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## Example 329

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

Melting Point: 268.5 - 270.5°C

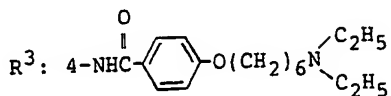
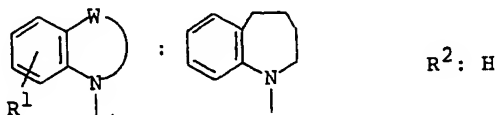
Form: Free

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Example 330

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

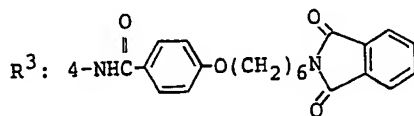
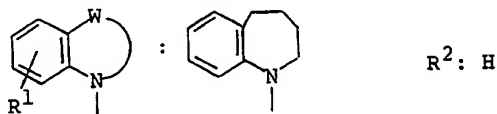
Melting Point: 174 - 176°C

Form: Hydrochloride

---

## Example 331

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 130 - 134°C

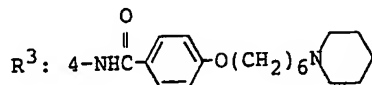
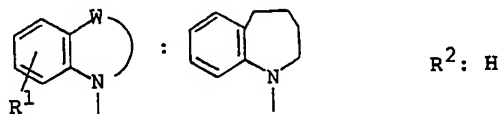
Form: Free

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Example 332

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

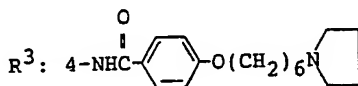
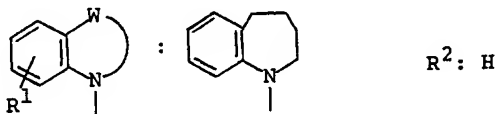
Melting Point: 214 - 217°C

Form: Hydrochloride

---

## Example 333

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 218 - 220°C

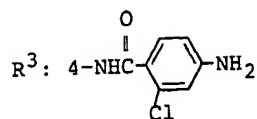
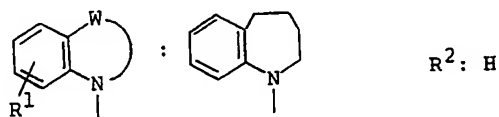
Form: Hydrochloride

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## Example 334

## Structure



Crystalline form: White powder

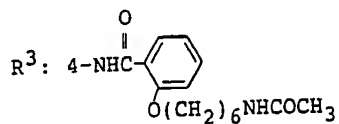
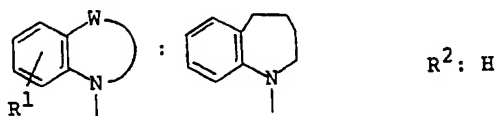
Recrystallization solvent: Ethyl acetate

Melting Point: 222 - 225°C

Form: Free

## Example 335

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Methanol/diethyl ether

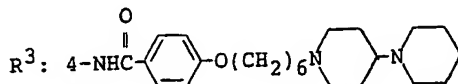
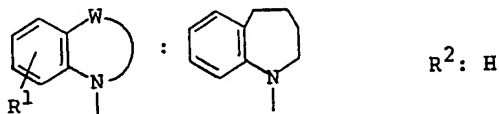
Melting Point: 171 - 172°C

Form: Free

---

Example 336

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

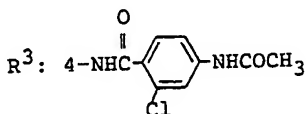
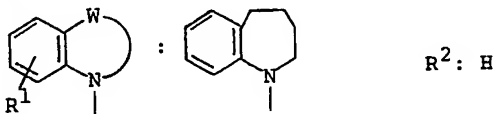
Melting Point: 235.5 - 236°C

Form: Dihydrochloride

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## Example 337

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 241 - 243°C

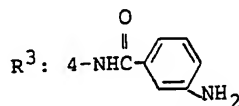
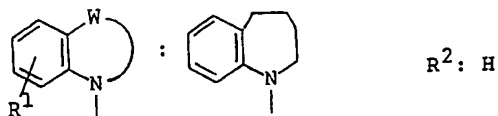
Form: Free

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Example 338

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

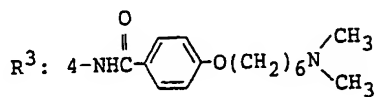
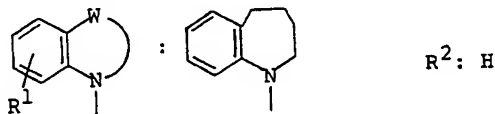
Melting Point: 187 - 191°C

Form: Free

---

## Example 339

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

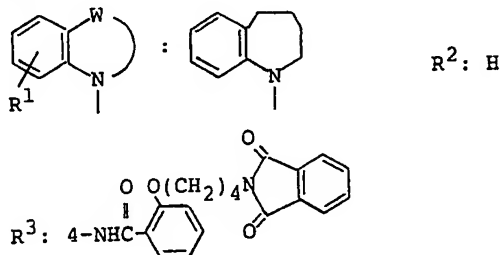
Melting Point: 240 - 244°C

Form: Hydrochloride

---

## Example 340

## Structure



Crystalline form: Colorless prisms

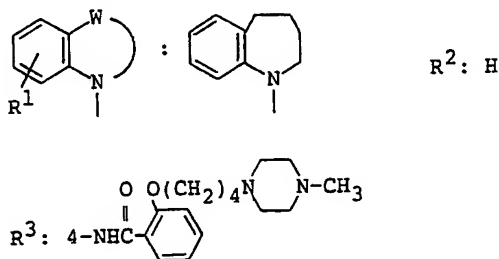
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 181 - 182°C

Form: Free

## Example 341

## Structure



Crystalline form: Colorless prisms

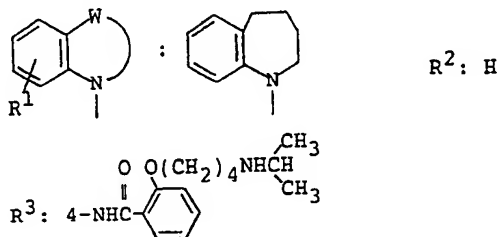
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 188 - 190°C

Form: Dihydrochloride

## Example 342

## Structure



Crystalline form: White powder

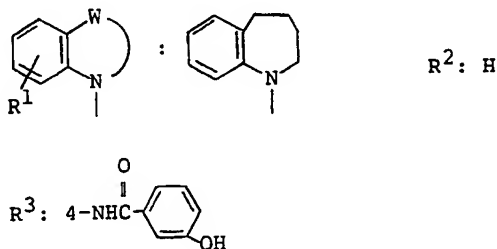
Recrystallization solvent: Isopropyl alcohol

Melting Point: 218 - 218.5°C

Form: Hydrochloride

## Example 343

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

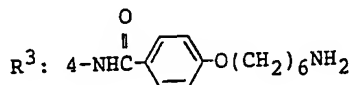
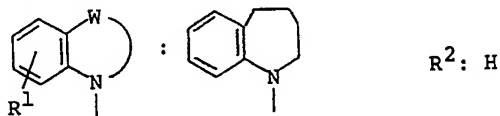
Melting Point: 243 - 245.5°C

Form: Free

---

Example 344

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

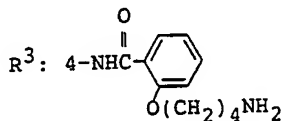
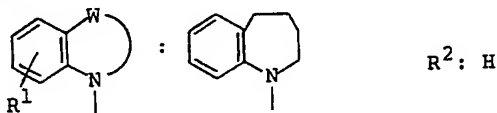
Melting Point: 130 - 133°C

Form: Free

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## Example 345

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

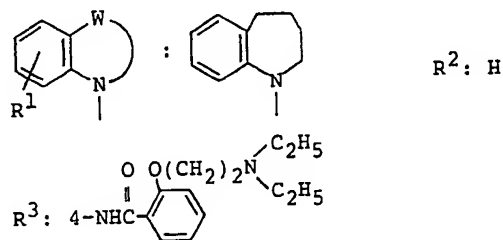
Melting Point: 155 - 158°C

Form: Free

---

## Example 346

## Structure



Crystalline form: White powder

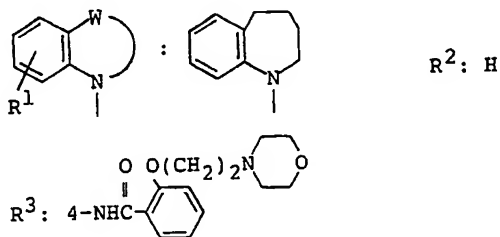
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 208 - 210°C

Form: Hydrochloride

## Example 347

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Methanol/diethyl ether

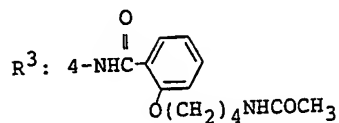
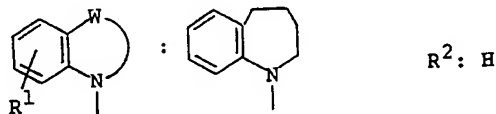
Melting Point: 154 - 155°C

Form: Hydrochloride

---

Example 348

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

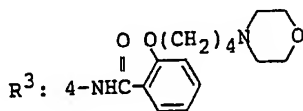
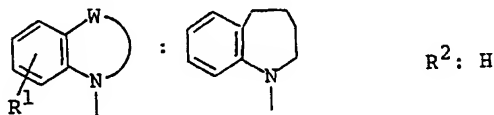
Melting Point: 142 - 143°C

Form: Free

---

## Example 349

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 120 - 125°C

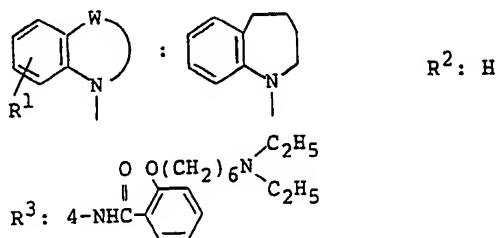
Form: Hydrochloride

---



## Example 350

## Structure



Crystalline form: White powder

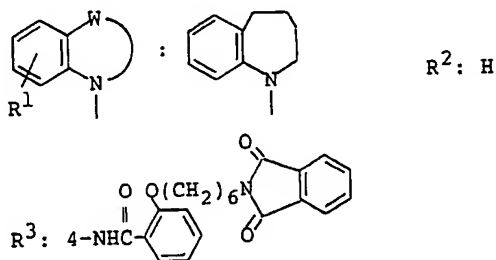
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 91 - 95°C

Form: Hydrochloride

## Example 351

## Structure



Crystalline form: White powder

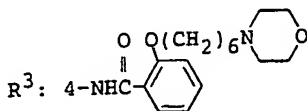
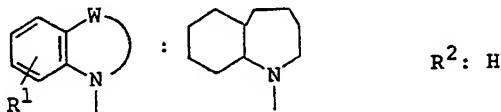
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 145 - 146.5°C

Form: Free

## Example 352

## Structure



Crystalline form: White powder

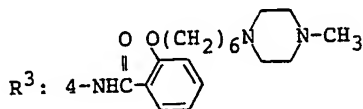
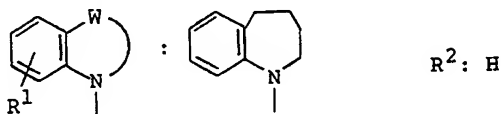
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 105 - 105.5°C

Form: Free

## Example 353

## Structure



Crystalline form: White powder

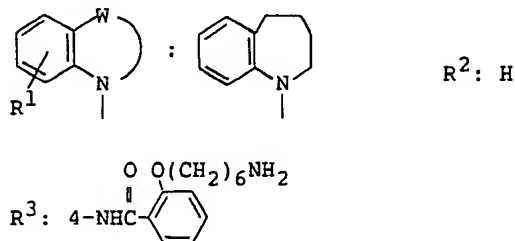
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 151 - 155°C

Form: Dihydrochloride

## Example 354

## Structure



Crystalline form: White powder

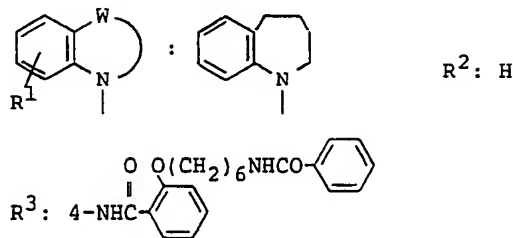
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 135.5 - 137.5°C

Form: Free

## Example 355

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

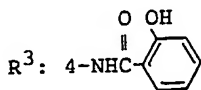
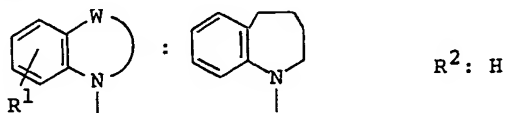
Melting Point: 178 - 178.5°C

Form: Free

---

Example 356

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane

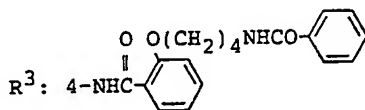
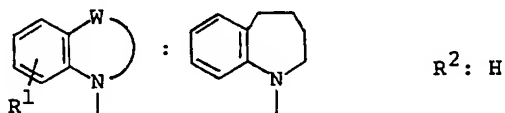
Melting Point: 266.5 - 268°C

Form: Free

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## Example 357

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 123 - 124°C

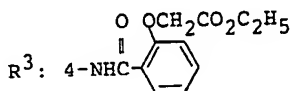
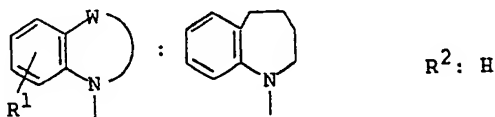
Form: Free

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Example 358

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

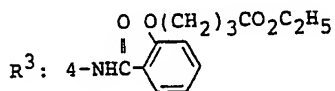
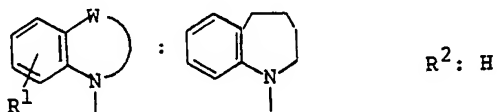
Melting Point: 212 - 213.5°C

Form: Free

---

## Example 359

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: Ethyl acetate

Melting Point: 160.5 - 162°C

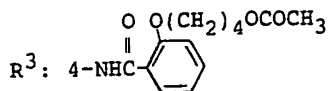
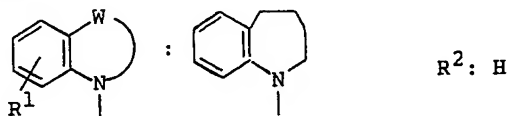
Form: Free

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Example 360

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

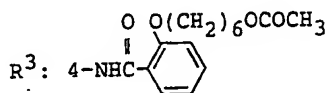
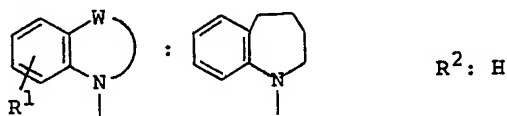
Melting Point: 103 - 105°C

Form: Free

---

## Example 361

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 145 - 146°C

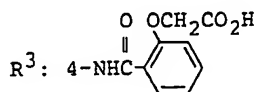
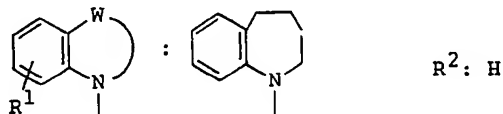
Form: Free

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Example 362

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

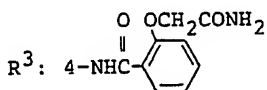
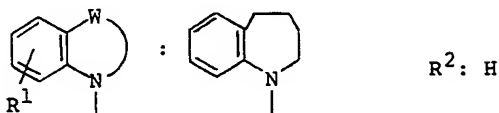
Melting Point: 247 - 250°C

Form: Free

---

## Example 363

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 198 - 199°C

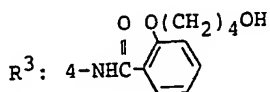
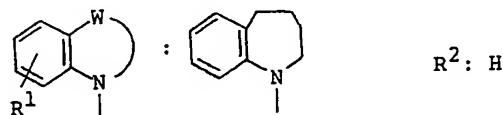
Form: Free

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Example 364

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

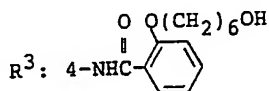
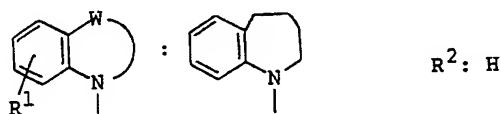
Melting Point: 181.5 - 182.5°C

Form: Free

---

## Example 365

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 170 - 170.5°C

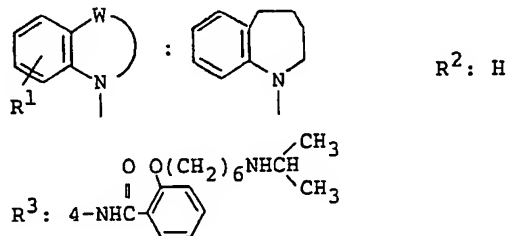
Form: Free

---



## Example 366

## Structure



Crystalline form: White powder

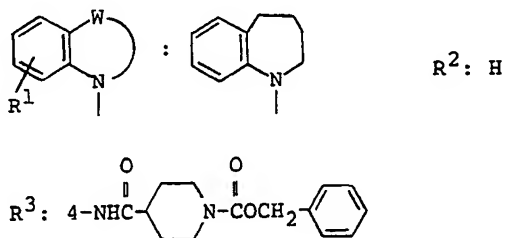
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 156 - 158°C

Form: Hydrochloride

## Example 367

## Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether

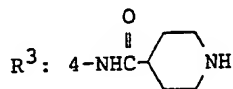
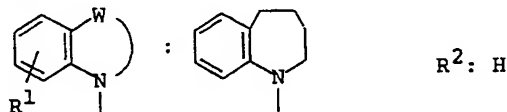
Melting Point: 168.5 - 170.5°C

Form: Free

---

Example 368

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

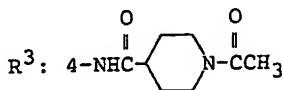
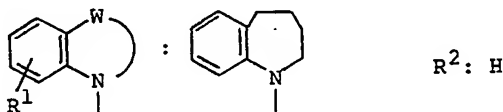
Melting Point: 177 - 181.5°C

Form: Hydrochloride

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## Example 369

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 211 - 213°C

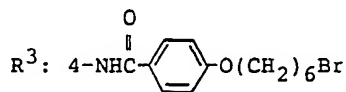
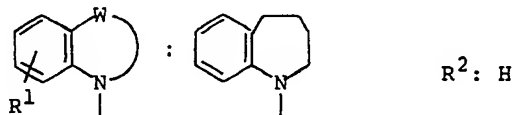
Form: Free

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Example 370

## Structure



Crystalline form: White powder

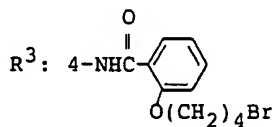
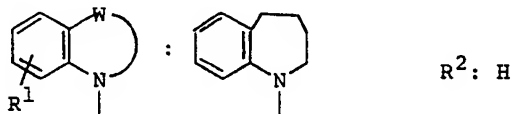
NMR analysis: 46)

Form: Free

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## Example 371

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/ethyl acetate

Melting Point: 166 - 167°C

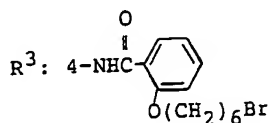
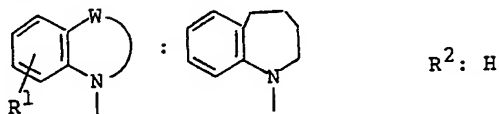
Form: Free

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Example 372

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

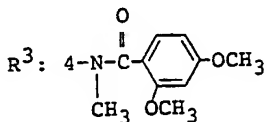
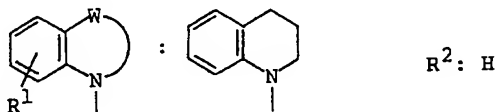
Melting Point: 127 - 131°C

Form: Free

---

## Example 373

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

Melting Point: 170 - 171°C

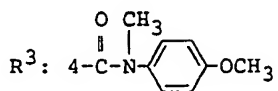
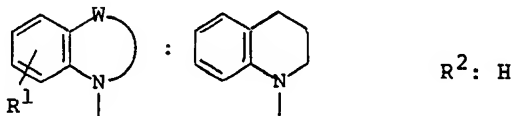
Form: Free

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Example 374

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol

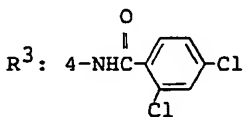
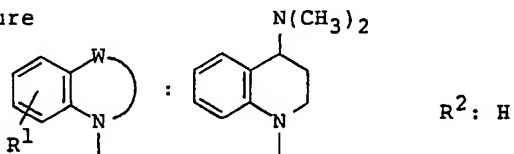
Melting Point: 125 - 126°C

Form: Free

---

## Example 375

## Structure



Crystalline form: Light yellow amorphous

NMR analysis: 47)

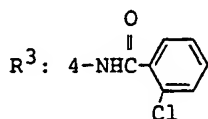
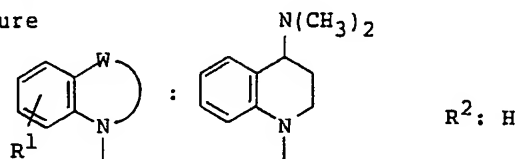
Form: Hydrochloride

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Example 376

Structure



Crystalline form: Colorless amorphous

NMR analysis: 48)

Form: Hydrochloride

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- 1)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.92 (1H, t,  $J=6.2$  Hz), 1.98 (1H, t,  $J=6.4$  Hz), 2.8 (2H, t,  $J=6.4$  Hz), 3.76 (2H, t,  $J=6.2$  Hz), 6.75 (1H, d,  $J=7.6$  Hz), 6.86 (2H, d,  $J=8.6$  Hz), 6.8-7.1 (2H, m), 7.20 (1H, d,  $J=7$  Hz), 7.30 (2H, d,  $J=8.6$  Hz), 7.72 (2H, d,  $J=8.6$  Hz), 7.84 (2H, d,  $J=8.6$  Hz), 10.13 (1H, s)
- 2)  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  : 2.05 (2H, quint,  $J=6.4$  Hz), 2.91 (2H, t,  $J=6.4$  Hz), 3.86 (2H, t,  $J=6.4$  Hz), 6.85 (1H, d,  $J=7.6$  Hz), 6.9-7.2 (2H, m), 7.30 (1H, d,  $J=7.2$  Hz), 7.44 (2H, d,  $J=8.5$  Hz), 7.85 (2H, d,  $J=8.5$  Hz), 8.1-8.2 (4H, m), 10.65 (1H, s), 13.2-13.4 (1H, br)
- 3)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.9-2.1 (2H, m), 2.84 (2H, t,  $J=6.5$  Hz), 3.82 (6H, s), 3.90 (2H, t,  $J=6.6$  Hz), 6.5-7.2 (7H, m), 7.35 (2H, d,  $J=8.7$  Hz), 7.55 (2H, d,  $J=8.7$  Hz), 8.05 (1H, s)
- 4)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.9-2.1 (2H, m), 2.37 (6H, s), 2.84 (2H, t,  $J=6.6$  Hz), 3.90 (2H, t,  $J=6.6$  Hz), 6.71 (1H, d,  $J=7.9$  Hz), 6.8-7.2 (4H, m), 7.35 (2H, d,  $J=8.6$  Hz), 7.44 (2H, s), 7.56 (2H, d,  $J=8.6$  Hz), 8.00 (1H, s)
- 5)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.9-2.2 (2H, m), 2.12 (3H, s), 2.84 (2H, t,  $J=6.6$  Hz), 3.89 (2H, t,  $J=6.5$  Hz), 6.71 (1H, d,  $J=7.8$  Hz), 6.87 (1H, t,  $J=7$  Hz), 6.99 (1H, t,  $J=7.3$  Hz), 7.15 (1H, d,  $J=6.5$  Hz), 7.28 (2H, d,  $J=8.6$  Hz), 7.41 (2H, d,  $J=8.6$  Hz), 8.03

- (1H, s)
- 6)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 0.8-1.3 (6H, m), 1.6-2.3 (9H, m), 2.83 (2H, t,  $J=6.6$  Hz), 3.89 (2H, t,  $J=6.5$  Hz), 6.72 (1H, d,  $J=7.9$  Hz), 6.8-7.1 (2H, m), 7.15 (1H, d,  $J=7.4$  Hz), 7.28 (2H, d,  $J=8.3$  Hz), 7.44 (2H, d,  $J=8.4$  Hz), 7.9-8.1 (1H, m)
- 7)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.02 (2H, quint,  $J=6.5$  Hz), 2.81 (2H, t,  $J=6.6$  Hz), 3.69 (2H, s), 3.87 (2H, t,  $J=6.6$  Hz), 6.66 (1H, d,  $J=8.2$  Hz), 6.8-7.0 (2H, m), 7.13 (1H, d,  $J=7.3$  Hz), 7.2-7.4 (9H, m), 7.59 (1H, s)
- 8)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.7-2.1 (17H, m), 2.83 (2H, t,  $J=6.7$  Hz), 3.90 (2H, t,  $J=6.6$  Hz), 6.68 (1H, d,  $J=8.1$  Hz), 6.8-7.1 (2H, m), 7.14 (1H, d,  $J=7$  Hz), 7.32 (2H, d,  $J=8.7$  Hz), 7.39 (1H, s), 7.46 (2H, d,  $J=8.7$  Hz)
- 9)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.99 (2H, quint,  $J=6.5$  Hz), 2.82 (2H, t,  $J=6.6$  Hz), 3.82 (2H, t,  $J=6.5$  Hz), 6.8-7.1 (4H, m), 7.1-7.3 (2H, m), 7.4-7.6 (3H, m), 7.67 (1H, s), 7.8-8.0 (3H, m), 8.42 (1H, s)
- 10)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.00 (2H, quint,  $J=6.5$  Hz), 2.83 (2H, t,  $J=6.6$  Hz), 3.85 (2H, t,  $J=6.6$  Hz), 3.86 (3H, s), 6.8-7.1 (6H, m), 7.1-7.3 (2H, m), 7.64 (1H, s), 7.8-8.0 (3H, m), 8.22 (1H, s)
- 11)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.98 (2H, quint,  $J=6.5$  Hz), 2.82 (2H, t,  $J=6.5$  Hz), 3.81 (2H, t,  $J=6.5$  Hz),



- 3.84 (3H, s), 6.8-7.5 (10H, m), 7.68 (1H, s), 7.95 (1H, d, J=8.2 Hz), 8.52 (1H, s)
- 12)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.7-1.9 (2H, m), 2.70 (2H, t, J=6.6 Hz), 3.70 (2H, t, J=6.4 Hz), 6.8-7.3 (6H, m), 7.4-7.7 (2H, m), 7.8-7.9 (5H, m), 8.04 (1H, d, J=8 Hz), 8.33 (1H, s), 8.90 (1H, s)
- 13)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.7-2.1 (17H, m), 2.84 (2H, t, J=6.5 Hz), 3.89 (2H, t, J=6.4 Hz), 6.8-7.2 (6H, m), 7.42 (1H, s), 7.56 (1H, s), 7.81 (1H, d, J=8.1 Hz)
- 14)  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  : 1.0-1.5 (5H, m), 1.5-2.0 (5H, m), 2.2-3.8 (8H, m), 4.2-5.2 (3H, m), 6.77 (1H, d, J=7.2 Hz), 7.1-7.4 (4H, m), 7.47 (2H, d, J=8.6 Hz), 7.58 (1H, d, J=6.2 Hz), 10.06 (1H, s), 10.9-12.1 (1H, br)
- 15)  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  : 2.5-3.8 (6H, m), 4.2-5.2 (3H, m), 6.81 (1H, d, J=6.8 Hz), 7.1-7.3 (4H, m), 7.5-7.7 (3H, m), 7.8-8.0 (1H, m), 7.97 (2H, d, J=1.8 Hz), 10.66 (1H, s), 11.1-12.3 (1H, br)
- 16)  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  : 2.20 (3H, s), 2.27 (3H, s), 2.5-3.8 (6H, m), 4.3-5.3 (3H, m), 6.82 (1H, d, J=7.2 Hz), 7.1-7.4 (7H, m), 7.5-7.8 (3H, m), 10.43 (1H, s), 11.0-12.2 (1H, br)
- 17)  $^1\text{H-NMR}$  ( $\text{DMCO-d}_6$ )  $\delta$  : 2.34 (3H, s), 2.5-3.7 (6H, m), 4.3-5.2 (3H, m), 6.82 (1H, d, J=6.8 Hz), 7.2-7.7 (11H, m), 10.41 (1H, s), 10.8-12.3 (1H, br)
- 18)  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  : 2.38 (3H, s), 2.5-3.8 (6H, m),

- 4.3-5.3 (3H, m), 6.81 (1H, d, J=7.0 Hz), 7.1-7.5 (6H, m), 7.5-7.8 (5H, m), 10.35 (1H, s), 10.9-12.2 (1H, br)
- 19)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 2.37 (3H, s), 2.5-3.7 (6H, m), 4.3-5.2 (3H, m), 6.81 (1H, d, J=7.2 Hz), 7.2-7.4 (6H, m), 7.5-7.7 (3H, m), 7.84 (2H, d, J=8.0 Hz), 10.31 (1H, s), 10.9-12.2 (1H, br)
- 20)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 2.5-3.8 (6H, m), 4.3-5.2 (3H, m), 6.82 (1H, d, J=7.4 Hz), 7.2-7.3 (4H, m), 7.5-7.8 (5H, m), 7.75 (1H, d, J=1.8 Hz), 10.70 (1H, s), 10.8-12.2 (1H, br)
- 21)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 2.5-3.8 (9H, m), 4.3-4.7 (1H, m), 4.7-5.1 (2H, m), 6.8-7.1 (3H, m), 7.1-7.4 (2H, m), 7.5-7.7 (2H, m), 7.8-8.0 (3H, m), 9.79 (1H, s), 10.8-12.2 (1H, br)
- 22)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 0.8-1.2 (3H, m), 1.7-2.2 (2H, m), 2.5-3.8 (5H, m), 4.3-5.2 (3H, m), 6.80 (1H, d, J=7.2 Hz), 7.1-7.3 (4H, m), 7.6-7.7 (3H, m), 7.85 (1H, s), 7.96 (2H, d, J=1.8 Hz), 10.62 (1H, s), 10.8-12.0 (1H, br)
- 23)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 0.8-1.1 (3H, m), 1.7-2.1 (2H, m), 2.37 (3H, s), 2.7-3.8 (5H, m), 4.4-5.2 (3H, m), 6.81 (1H, d, J=7.6 Hz), 7.2-7.4 (6H, m), 7.6-7.7 (3H, m), 7.84 (2H, d, J=8.2 Hz), 10.29 (1H, s), 10.5-11.8 (1H, br)
- 24)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 0.8-1.2 (3H, m), 1.7-2.1 (2H,

- m), 2.38 (3H, s), 2.6-3.8 (5H, m), 4.3-5.2 (3H, m), 6.81 (1H, d, J=7.0 Hz), 7.2-7.5 (6H, m), 7.6-7.8 (5H, m), 10.33 (1H, s), 10.5-11.7 (1H, br)
- 25)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 0.8-1.2 (3H, m), 1.7-2.1 (2H, m), 2.6-3.8 (5H, m), 3.8-5.2 (3H, m), 6.82 (1H, d, J=7.2 Hz), 7.1-7.5 (8H, m), 7.5-7.7 (3H, m), 10.42 (1H, s), 10.7-12.0 (1H, br)
- 26)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 0.8-2.0 (15H, m), 2.2-2.5 (1H, m), 2.6-3.7 (5H, m), 4.3-5.2 (3H, m), 6.76 (1H, d, J=7.0 Hz), 7.1-7.4 (4H, m), 7.46 (2H, d, J=8.6 Hz), 7.61 (1H, d, J=6.4 Hz), 10.03 (1H, s), 10.5-11.8 (1H, br)
- 27)  $^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 0.8-1.1 (3H, m), 1.7-2.0 (2H, m), 2.20 (3H, s), 2.29 (3H, s), 2.6-3.7 (5H, m), 4.3-5.2 (3H, m), 6.82 (1H, d, J=7.0 Hz), 7.2-7.4 (7H, m), 7.5-7.7 (3H, m), 10.41 (1H, s), 10.6-12.0 (1H, br)
- 28)  $^1\text{H-NMR}$  (CDCl $_3$ )  $\delta$  : 1.21 (3H, t, J=7.1 Hz), 3.00-3.25 (3H, m), 4.00-4.30 (4H, m), 6.63 (1H, d, J=7.8 Hz), 6.86 (1H, t, J=7.3 Hz), 7.00 (1H, t, J=6.3 Hz), 7.10-7.31 (3H, m), 7.40-7.57 (3H, m), 7.77 (2H, d, J=1.9 Hz), 8.76 (1H, brs)
- 29)  $^1\text{H-NMR}$  (CDCl $_3$ )  $\delta$  : 2.29 (3H, s), 2.32 (3H, s), 2.34 (3H, s), 2.50-3.15 (11H, m), 3.79 (1H, dd, J=13.2 Hz, 7.3 Hz), 4.05 (1H, dd, J=13.2 Hz, 5.7 Hz), 6.62 (1H, d, J=7.7 Hz), 6.82-7.48 (8H, m), 7.53 (2H, d,

- J=8.4 Hz), 8.05 (1H, brs)
- 30)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.65-2.01 (4H, m), 2.31 (3H, s), 2.35 (3H, s), 2.55-3.02 (6H, m), 3.09 (1H, dd, J=15 Hz, 5 Hz), 3.70 (1H, dd, J=12.5 Hz, 8.0 Hz), 4.22 (1H, dd, J=12.5 Hz, 5 Hz), 6.67 (1H, d, J=7.8 Hz), 6.80-7.32 (7H, m), 7.37 (2H, d, J=8.6 Hz), 7.53 (1H, d, J=8.3 Hz), 7.66 (1H, brs)
- 31)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.80 (1H, dd, J=16.1 Hz, 5.3 Hz), 3.16 (1H, dd, J=15.8 Hz, 5.3 Hz), 3.75-4.50 (3H, m), 4.87-5.10 (3H, m), 6.80-7.60 (14H, m), 7.74 (2H, d, J=1.9 Hz), 8.47 (1H, brs)
- 32)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.35 (6H, s), 2.72-3.10 (3H, m), 3.65-3.78 (1H, m), 4.06-4.18 (1H, m), 6.60-7.62 (9H, m), 7.74 (2H, d, J=1.8 Hz), 8.52 (1H, brs)
- 33)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.87 (3H, s), 2.68 (1H, dd, J=5.6 Hz, 16 Hz), 3.14 (1H, dd, J=5.6 Hz, 16 Hz), 3.70-3.95 (2H, m), 4.32-4.50 (1H, m), 6.29 (1H, d, J=7.6 Hz), 6.90-7.80 (11H, m), 9.16 (1H, brs)
- 34)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.62 (1H, brs), 1.90-2.25 (2H, m), 2.55 (3H, s), 3.78 (1H, t, J=5.1 Hz), 3.95 (2H, t, J=6.7 Hz), 6.69 (1H, t, J=7.9 Hz), 6.90-7.13 (2H, m), 7.23-7.40 (3H, m), 7.42-7.56 (3H, m), 7.77 (2H, d, J=1.9 Hz), 8.53 (1H, brs)
- 35)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.80-2.02 (1H, m), 2.20-2.35 (1H, m), 2.31 (6H, s), 3.52 (1H, t, J=5.4 Hz), 3.68-3.83 (1H, m), 3.95-4.15 (1H, m), 6.59 (1H, d,

- J=7.8 Hz), 6.81-7.10 (2H, m), 7.16-7.50 (6H, m),  
7.80 (2H, d, J=1.8 Hz), 9.13 (1H, brs)
- 36)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.35-1.60 (1H, m), 1.65-2.20  
(3H, m), 2.65-3.20 (5H, m), 3.81 (2H, d, J=6.5 Hz),  
4.90-5.10 (1H, m), 6.60 (1H, d, J=8.0 Hz), 6.90  
(1H, t, J=8.0 Hz), 7.00-7.50 (6H, m)
- 37)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.30-2.25 (4H, m), 2.55-3.20  
(3H, m), 3.35 (2H, s), 3.80 (2H, s), 4.90-5.10 (1H,  
m), 6.62 (1H, d, J=8.0 Hz), 6.85-7.45 (12H, m),  
9.27 (1H, brs)
- 38)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.35-2.25 (4H, m), 2.33 (3H, s),  
2.60-3.20 (3H, m), 3.12 (2H, s), 3.61 (2H, s), 5.00  
(1H, brs), 6.50-7.60 (13H, m), 9.14 (1H, brs)
- 39)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.27 (3H, t, J=7.1 Hz), 1.25-  
2.50 (12H, m), 2.70-3.10 (4H, m), 3.05 (2H, s),  
4.15 (2H, q, J=7.0 Hz), 4.90-5.10 (1H, m), 6.63  
(1H, d, J=7.5 Hz), 6.91 (1H, t, J=7.5 Hz), 7.00-  
7.50 (6H, m), 9.14 (1H, brs)
- 40)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.30-1.65 (1H, m), 1.80-2.25  
(5H, m), 2.70-3.20 (3H, m), 4.01 (2H, d, J=5.0 Hz),  
4.90-5.10 (1H, m), 6.61 (1H, d, J=7.7 Hz), 6.89  
(1H, t, J=7.0 Hz), 7.00-7.45 (6H, m), 9.05 (1H,  
brs)
- 41)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.18 (6H, s), 1.30-2.20 (4H, m),  
2.60-3.20 (3H, m), 3.30 (2H, s), 3.73 (2H, s),  
4.90-5.10 (1H, m), 6.61 (1H, d, J=7.3 Hz), 6.70-

- 7.45 (12H, m), 9.50 (1H, brs)
- 42)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.19 (3H, t,  $J=7.0$  Hz), 1.30-1.70 (1H, m), 1.75-2.20 (3H, m), 2.65-3.15 (3H, m), 3.46 (2H, q,  $J=7.0$  Hz), 3.88 (2H, s), 4.90-5.10 (1H, m), 6.55-7.45 (13H, m), 8.36 (1H, brs)
- 43)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.08 (3H, t,  $J=7.2$  Hz), 1.05-2.25 (14H, m), 2.25-3.25 (10H, m), 4.90-5.10 (1H, m), 6.64 (1H, d,  $J=7.6$  Hz), 6.90 (1H, t,  $J=7.2$  Hz), 6.94-7.50 (6H, m), 11.50 (1H, brs)
- 44)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.06 (3H, t,  $J=7.5$  Hz), 1.30-2.20 (6H, m), 2.60-3.20 (3H, m), 3.65 (1H, m), 3.95 (1H, brs), 4.90-5.10 (1H, m), 6.50-6.75 (3H, m), 6.75-7.05 (2H, m), 7.05-7.55 (8H, m), 8.67 (1H, brs)
- 45)  $^1\text{H-NMR}$  ( $\text{DMSO}-d_6$ )  $\delta$  : 1.28-1.57 (1H, m), 1.69-2.20 (3H, m), 2.59-3.15 (3H, m), 4.74-4.98 (1H, m), 6.62-6.80 (1H, m), 6.86-7.37 (5H, m), 7.50-7.70 (2H, m), 8.95-9.02 (1H, m), 9.03-9.15 (2H, m), 10.85 (1H, s)
- 46)  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.40-1.66 (5H, m), 1.72-2.20 (7H, m), 2.63-3.18 (3H, m), 3.42 (2H, t,  $J=6.7$  Hz), 4.00 (2H, t,  $J=6.3$  Hz), 4.91-5.13 (1H, m), 6.58-6.72 (1H, m), 6.82-7.00 (3H, m), 7.02-7.30 (4H, m), 7.36-7.51 (2H, m), 7.70-7.88 (2H, m), 7.91 (1H, s)
- 47)  $^1\text{H-NMR}$  ( $\text{DMSO}-d_6$ )  $\delta$  : 2.05-2.95 (8H, m), 3.43-3.70 (1H, m), 4.08-4.30 (1H, m), 4.72-5.00 (1H, m),

6.70-8.08 (11H, m), 10.8 (1H, s), 11.1 (1H, brs)  
48)  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$  : 2.10-3.00 (8H, m), 3.47-3.70  
(1H, m), 4.07-4.33 (1H, m), 4.75-4.98 (1H, m),  
6.78-6.91 (1H, m), 7.05-7.22 (2H, m), 7.30-7.97  
(9H, m), 10.75 (1H, s), 10.94 (1H, brs)

Example 377

To a solution of 1-[4-(4-formylbenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.3 g) in methanol (10 ml) is added gradually sodium borohydride (59 mg) under ice-cooling and the mixture is stirred at room temperature for 2 hours. Water is added to the mixture and the solvent is distilled off under reduced pressure. The resulting residue is extracted with dichloromethane, washed with water, and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1), and recrystallized from methanol to give 1-[4-(4-hydroxymethylbenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (165 mg) as white powder, m.p. 224.5 - 225.5°C.

Using the suitable starting materials, the compound of the above Example 37 is obtained in the same manner as in Example 377.

Example 378

To a solution of 1-[4-(4-methoxycarbonylbenzoyl)-

amino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) in methanol (20 ml) is added 5 % aqueous sodium hydroxide solution (10 ml) and the mixture is stirred at room temperature overnight. Methanol is distilled off under reduced pressure and the resulting residue is acidified with diluted aqueous hydrochloric acid solution. The precipitated crystal is collected by filtration to give 1-[4-(4-carboxybenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) as white powder, m.p. >300°C.

$^1\text{H-NMR}$  (DMSO- $d_6$ )  $\delta$  : 2.05 (2H, quint,  $J=6.4$  Hz), 2.91 (2H, t,  $J=6.4$  Hz), 3.86 (2H, t,  $J=6.4$  Hz), 6.85 (1H, d,  $J=7.6$  Hz), 6.9-7.2 (2H, m), 7.30 (1H, d,  $J=7.2$  Hz), 7.44 (2H, d,  $J=8.5$  Hz), 7.85 (2H, d,  $J=8.5$  Hz), 8.1-8.2 (4H, m), 10.65 (1H, s), 13.2-13.4 (1H, br)

Using the suitable starting materials, the compounds of the above Examples 39, 241, 252, 253 and 362 are obtained in the same manner as in Example 378.

#### Example 379

To a solution of 1-[4-(3-acetyloxybenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (1.5 g) in methanol (20 ml) is added 5 % aqueous sodium hydroxide solution (10 ml) and the mixture is stirred at room temperature overnight. Methanol is distilled off under reduced pressure and the resulting residue is acidified with diluted aqueous hydrochloric acid solution. The precipitated crystal is collected by filtration and recrystallized from methanol to



give 1-[4-(3-hydroxybenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (1.22 g) as white powder, m.p. 217 - 218°C.

Using the suitable starting materials, the compounds of the above Examples 10, 343, 356, 364 and 365 are obtained in the same manner as in Example 379.

Example 380

To a solution of 1-[4-(3-hydroxybenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) in acetone (5 ml) are added potassium carbonate (0.22 g) and ethyl iodide (0.34 g), and the mixture is refluxed for 5 hours. Then, acetone is distilled off under reduced pressure and water is added to the residue. The precipitated crystal is collected by filtration, and recrystallized from methanol to give 1-[4-(3-ethoxybenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.36 g) as white powder, m.p. 170.5 - 171.5°C.

Using the suitable starting materials, the compounds of the above Examples 11, 12, 13, 14, 33, 35, 48, 50 - 55, 90 - 92, 97 - 100, 109 - 111, 120 - 122, 136 - 138, 165 - 167, 175 - 177, 192 - 194, 211, 212, 214, 321, 322, 330 - 333, 335, 336, 339 - 342, 344 - 355, 357 - 366 and 370 - 374 are obtained in the same manner as in Example 380.

Example 381

Ethanol (50 ml) is added to 10 % Pd-C (0.1 g) and thereto is added 1-[4-(3-nitrobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.73 g). The mixture is subjected to

catalytic reduction at ordinary temperature under atmospheric pressure of hydrogen. After completion of the reduction, 10 % Pd-C is removed by filtration and the filtrate is concentrated under reduced pressure. The residue is extracted with dichloromethane and the extract is dried over magnesium sulfate. The solvent is distilled off under reduced pressure and recrystallized from methanol to give 1-[4-(3-aminobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.54 g) as white powder, m.p. 205.5 - 206.5°C.

Using the suitable starting materials, the compounds of the above Examples 24, 334 and 338 are obtained in the same manner as in Example 381.

#### Example 382

To a solution of 1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (0.5 g) in dichloromethane (20 ml) is added triethylamine (0.3 g), and thereto is added benzoyl chloride (0.28 g) under ice-cooling. The mixture is stirred at room temperature for 1 hour. To the reaction mixture is added water and extracted with dichloromethane. The extract is dried over magnesium sulfate and the solvent is distilled off under reduced pressure. The resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1) and recrystallized from methanol to give 1-[4-(benzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (245 mg) as white powder, m.p. 202.5 - 203.5°C.

Using the suitable starting materials, the compounds of the above Examples 2 - 119, 131 - 373, 375 and 376 are obtained in the same manner as in Example 382.

Example 383

Thionyl chloride (10 ml) is added to 1-(4-carboxy-benzoyl)-1,2,3,4-tetrahydroquinoline (0.5 g) and the mixture is refluxed for 1 hour. Thionyl chloride is distilled off under reduced pressure to give 4-[1-(1,2,3,4-tetrahydroquinolyl)carbonyl]benzoyl chloride. Separately, to a solution of m-anisidine (0.27 g) in dichloromethane (20 ml) is added triethylamine (0.34 g), and thereto is added gradually the above obtained 4-[1-(1,2,3,4-tetrahydroquinolyl)carbonyl]benzoyl chloride under ice-cooling and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the mixture is extracted with dichloromethane. The extract is dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1), and recrystallized from methanol to give 1-[4-(3-methoxyanilinocarbonyl)benzoyl]-1,2,3,4-tetrahydroquinoline (203 mg) as colorless needles, m.p. 154 - 155°C.

Using the suitable starting materials, the compounds of the above Examples 120, 122 - 130 and 374 are obtained in the same manner as in Example 383.

Example 384

To 4-oxo-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.7 g) are added tetrahydrofuran (10 ml) and methanol (10 ml). To the mixture is added sodium borohydride (0.1 g) in portions and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the mixture is extracted with dichloromethane. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane + dichloromethane : methanol = 20 : 1), and recrystallized from ethanol to give 4-hydroxy-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) as white powder, m.p. 215 - 217°C.

#### Example 385

To 3-ethoxycarbonyl-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.6 g) are added an aqueous solution of sodium hydroxide (0.1 g) in water (1 ml) and ethanol (5 ml). The mixture is stirred at room temperature for 15 minutes, and acidified with diluted hydrochloric acid, extracted with dichloromethane. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane + dichloromethane : methanol = 50 : 1), and recrystallized from ethanol to give 3-carboxy-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.4 g) as white powder, m.p. 221 - 223°C.

Example 386

To 3-carboxy-1-[4-(3,5-dichlorobenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (3.7 g) are added tetrahydrofuran (50 ml) and thionyl chloride (5 ml). The mixture is reacted at 60°C for 1 hour. The reaction mixture is concentrated and to the residue is added acetone (20 ml). To the mixture is added dropwise a solution of sodium azide (1.0 g) in water (5 ml) under ice-cooling. The reaction mixture is stirred at the same temperature for 30 minutes and extracted with dichloromethane, dried over magnesium sulfate. The solvent is concentrated and to the resulting residue are added anhydrous toluene (30 ml) and benzyl alcohol (1.7 g). The mixture is refluxed for 1 hour. The reaction mixture is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane + dichloromethane : methanol = 50 : 1) to give 3-benzyloxycarbonylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (3.7 g) as colorless amorphous.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.80 (1H, dd,  $J=16.1$  Hz, 5.3 Hz), 3.16 (1H, dd,  $J=15.8$  Hz, 5.3 Hz), 3.75-4.50 (3H, m), 4.87-5.10 (3H, m), 6.80-7.60 (14H, m), 7.74 (2H, d,  $J=1.9$  Hz), 8.47 (1H, brs)

Example 387

To 3-benzyloxycarbonylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (3.3 g)

are added acetic acid (40 ml) and 10 % Pd-C (0.4 g) and the reaction mixture is subjected to catalytic reduction at ordinary temperature under atmospheric pressure of hydrogen. One hour thereafter, the catalyst is removed by filtration and the filtrate is concentrated. The resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 20 : 1), and recrystallized from ethanol to give 3-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (1.6 g) as white powder, m.p. 207 - 210°C.

Example 388

To 3-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) are added methanol (10 ml), 37 % formaline (0.8 ml) and sodium cyanoborohydride (0.16 g). To the mixture is added acetic acid (0.5 ml) under ice-cooling and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the mixture is basified with potassium carbonate and extracted with dichloromethane. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane + dichloromethane : methanol = 20 : 1) to give 3-dimethyl-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.3 g) as colorless amorphous.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 2.35 (6H, s), 2.72-3.10 (3H, m), 3.65-3.78 (1H, m), 4.06-4.18 (1H, m), 6.60-7.62 (9H, m),

7.74 (2H, d, J=1.8 Hz), 8.52 (1H, brs)

Using the suitable starting materials, the compounds of the above Examples 246, 247, 375 and 376 are obtained in the same manner as in Example 388.

Example 389

To 3-amino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.44 g) are added dichloromethane (5 ml) and acetic anhydride (0.12 g) and the mixture is stirred for 1 hour. The reaction mixture is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane + dichloromethane : methanol = 50 : 1) to give 3-acetylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.3 g) as colorless amorphous.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.87 (3H, s), 2.68 (1H, dd, J=5.6 Hz, 16 Hz), 3.14 (1H, dd, J=5.6 Hz, 16 Hz), 3.70-3.95 (2H, m), 4.32-4.50 (1H, m), 6.29 (1H, d, J=7.6 Hz), 6.90-7.80 (11H, m), 9.16 (1H, brs)

Using the suitable starting materials, the compound of the above Example 242 is obtained in the same manner as in Example 389.

Example 390

To 4-oxo-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) are added 40 % solution of methylamine in methanol (5 ml), molecular sieves 4A (1 g) and dimethylformamide (6 ml), and the mixture is refluxed

for 4 hours. After cooling, the reaction mixture is filtered and to the filtrate is added sodium borohydride (80 mg), and the mixture is stirred at room temperature for 1 hour. The reaction mixture is concentrated and water is added to the resulting residue, and extracted with ethyl acetate. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 20 : 1) to give 4-methylamino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline (0.2 g) as colorless amorphous.

$^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$  : 1.62 (1H, brs), 1.90-2.25 (2H, m), 2.55 (3H, s), 3.78 (1H, t,  $J=5.1$  Hz), 3.95 (2H, t,  $J=6.7$  Hz), 6.99 (1H, d,  $J=7.9$  Hz), 6.90-7.13 (2H, m)

Using the suitable starting materials, the compounds of the above Examples 238, 239, 244, 247, 375 and 376 are obtained in the same manner as in Example 390.

#### Example 391

To 3-carboxy-1-[4-(3,5-dichlorobenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.7 g) are added dimethylformamide (7 ml), diethyl cyanophosphate (0.3 ml) and dimethylamine hydrochloride (0.15 g). Further thereto is added triethylamine (0.8 ml) and the mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and extracted with ethyl acetate. The solvent is concentrated and to the resulting residue is added diethyl ether. The precipitated crystal is collected by filtration



to give 3-dimethylamido-1-[4-(3,5-dichlorobenzoylamino)-benzoyl]-1,2,3,4-tetrahydroquinoline (0.5 g) as light yellow powder, m.p. 186 - 187°C.

#### Example 392

To a solution of 1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (3.0 g) in dichloromethane (50 ml) is added succinic anhydride (1.4 g) and the mixture is stirred at room temperature for 4.5 hours. The reaction mixture is evaporated under reduced pressure in order to remove the solvent therefrom, and the resulting crystal is recrystallized from ethyl acetate to give 1-[4-(3-carboxypropionylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (3.61 g) as colorless needles, m.p. 192°C.

Using the suitable starting materials, the compound of the above Example 253 is obtained in the same manner as in Example 392.

#### Example 393

1-[4-(3-Carboxypropionylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.5 g) is dissolved in dimethylformamide (1 ml) and thereto is added dropwise diethyl cyanophosphate (0.25 g) under ice-cooling. The mixture is stirred at room temperature for 30 minutes and then cooled again with ice. Thereto are added dropwise a solution of diethylamine (0.11 g) in dimethylformamide (1 ml) and triethylamine (0.34 g). The mixture is stirred at room temperature for 16 hours. The solvent is distilled off

under reduced pressure and water is added to the resulting residue. The mixture is extracted with dichloromethane. The organic layer is washed successively with diluted hydrochloric acid, water, saturated sodium hydrogen carbonate solution, water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; ethyl acetate), and recrystallized from n-hexane/ethyl acetate to give 1-[4-(3-diethylaminocarbonylpropionylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.42 g) as colorless scales, m.p. 165 - 167°C.

Using the suitable starting materials, the compounds of the above Examples 255 - 263 are obtained in the same manner as in Example 393.

Example 394

To a solution of 1-[4-(2-chloroacetylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (2.06 g) in dimethylformamide (5 ml) are added sodium iodide (0.90 g), potassium carbonate (1.1 g) and cyclohexylamine (0.89 g), and the mixture is stirred at room temperature for 2 hours. Dimethylformamide is distilled off under reduced pressure and water is added to the resulting residue. The mixture is extracted with dichloromethane. The organic layer is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is

distilled off under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; ethyl acetate), and recrystallized from n-hexane/-ethyl acetate to give 1-[4-(2-cyclohexylaminoacetyl-amino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (2.03 g) as white powder, m.p. 139 - 142°C.

Using the suitable starting materials, the compounds of the above Examples 271 - 309 and 317 are obtained in the same manner as in Example 394.

#### Example 395

o-Cresol (0.36 g) is dissolved in dimethylsulfoxide (4 ml) containing sodium hydroxide powder (0.18 g) and thereto is added 1-[4-(2-chloroacetyl-amino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (1.03 g). The mixture is stirred at 90°C for 7.5 hours. The reaction mixture is poured into ice-water (300 ml) and the precipitated crystal is collected by filtration, washed with water, and purified by silica gel column chromatography (eluent; n-hexane : ethyl acetate = 2 : 1), and recrystallized from ethyl acetate to give 1-[4-(2-(2-methylphenoxy)acetyl-amino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (546 mg) as colorless scales, m.p. 172.5 - 175°C.

Using the suitable starting materials, the compounds of the above Examples 310 and 312 - 316 are obtained in the same manner as in Example 395.

#### Example 396

A mixture of 1-[4-[2-(6-bromohexyloxy)benzoyl]-

amino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (2.00 g), sodium acetate (0.36 g), sodium iodide (0.55 g) and acetic acid (20 ml) is refluxed for 1 day. The solvent is distilled off and the resulting residue is extracted with ethyl acetate. The organic layer is washed successively with 2N aqueous sodium hydroxide solution and saturated saline solution, and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 500 : 1), and recrystallized from ethanol to give 1-{4-[2-(6-acetyloxyhexyloxy)benzoylamino]-benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (1.07 g) as white powder, m.p. 145 - 146°C.

Using the suitable starting materials, the compound of the above Example 360 is obtained in the same manner as in Example 396.

#### Example 397

A mixture of 1-{4-[2-(6-bromoheptyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g), diethylamine (0.16 ml), triethylamine (0.21 ml) and acetonitrile (20 ml) is refluxed overnight. The solvent is distilled off and the resulting residue is dissolved in chloroform, washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent;

chloroform : methanol = 200 : 1 + 50 : 1) and converted into the hydrochloride thereof in methanol. The product is recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-diethylaminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine hydrochloride (0.42 g) as white powder, m.p. 91 - 95°C.

Using the suitable starting materials, the compounds of the above Examples 330, 332, 333, 335, 336, 339, 341, 342, 344 - 349, 352 - 355, 357 and 366 are obtained in the same manner as in Example 397.

#### Example 398

A mixture of 1-{4-[2-(6-bromohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (4.00 g), potassium phthalimide (2.02 g) and dimethylformamide (100 ml) is stirred at 100°C for 5 hours. The reaction mixture is filtered and the filtrate is distilled off. The resulting residue is extracted with ethyl acetate and the organic layer is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; dichloromethane), and recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-phthalimidohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (4.06 g) as white powder, m.p. 145 - 146.5°C.

Using the suitable starting materials, the

compounds of the above Examples 331, 340, 364 and 365 are obtained in the same manner as in Example 398.

#### Example 399

A mixture of 1-{4-[2-(6-phthalimidohexyloxy)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (3.75 g), hydrazine hydrate (0.44 ml) and ethanol (30 ml) is refluxed for 3.5 hours. The precipitated crystal is collected by filtration, dried and purified by silica gel column chromatography (eluent; chloroform : methanol : aqueous ammonia = 100 : 10 : 1), and recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-aminohexyloxy)-benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (2.52 g) as white powder, m.p. 135.5 - 137.5°C.

Using the suitable starting materials, the compounds of the above Examples 284, 344 and 345 are obtained in the same manner as in Example 399.

#### Example 400

A mixture of 1-{4-[2-(6-aminohexyloxy)benzoyl-amino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g), acetic anhydride (20 ml) and two drops of conc. sulfuric acid is stirred at room temperature for 3 hours. To the reaction mixture is added aqueous 2N aqueous sodium hydroxide solution under ice-cooling and the mixture is extracted with chloroform. The organic layer is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off

and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 200 : 1), and recrystallized from methanol/diethyl ether to give 1-{4-[2-(6-acetylaminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.60 g) as colorless needles, m.p. 171 - 172°C.

#### Example 401

A mixture of 1-{4-[2-(6-aminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g), benzoyl chloride (0.20 ml), triethylamine and dichloromethane (20 ml) is stirred at room temperature for 1 hour. The reaction mixture is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is recrystallized from ethanol to give 1-{4-[2-(6-benzoylaminohexyloxy)benzoylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.71 g) as white powder, m.p. 178 - 178.5°C.

Using the suitable starting materials, the compounds of the above Examples 348 and 357 are obtained in the same manner as in Examples 400 and 401.

#### Example 402

A mixture of 1-{4-(2-ethoxycarbonylmethoxybenzoylamino)benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (1.00 g), aqueous ammonia (100 ml), ammonium chloride (0.3 g) and methanol (150 ml) is heated at 100°C for 4 hours in a sealed

tube. The solvent is distilled off and the resulting residue is extracted with chloroform, washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 50 : 1), and recrystallized from methanol/diethyl ether to give 1-[4-(2-carbamoylmethoxybenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.43 g) as white powder, m.p. 198 - 199°C.

#### Example 403

A mixture of 1-[4-(2-chloro-4-aminobenzoylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.55 g), acetic anhydride (15 ml), acetic acid (5 ml) and a drop of sulfuric acid is stirred at room temperature for 1 hour. To the reaction mixture is added aqueous 2N aqueous sodium hydroxide solution and the mixture is extracted with chloroform. The extract is washed with saturated saline solution and dried over magnesium sulfate. The solvent is concentrated and the resulting residue is recrystallized from methanol/diethyl ether to give 1-[4-(2-chloro-4-acetylaminobenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.28 g) as white powder, m.p. 214 - 243°C.

Using the suitable starting materials, the compound of the above Example 44 is obtained in the same manner as in Example 403.

#### Example 404



A mixture of 1-[4-(1-benzyloxycarbonyl-4-piperidinylcarbonylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (8.00 g), 10 % Pd-C (0.8 g) and ethanol (250 ml) is subjected to catalytic hydrogenation at 50°C under 4 atm. of hydrogen pressure for 6 hours. The catalyst is removed by filtration and the filtrate is evaporated under reduced pressure. The resulting residue is extracted with ethyl acetate and washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol : ammonium hydroxide = 50 : 10 : 1) to give 1-[4-[4-(4-piperidinyl)benzoylamino]benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (4.80 g), and a part (0.5 g) thereof is converted into the hydrochloride thereof in methanol. The hydrochloride is recrystallized from methanol/diethyl ether to give 1-[4-[4-(4-piperidinyl)-benzoylamino]benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine hydrochloride (0.42 g) as white powder, m.p. 177 - 181.5°C.

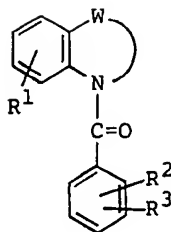
#### Example 405

Using the suitable starting materials, the following compound is obtained in the same manner as in the above Examples 1, 382 and 388.

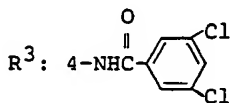
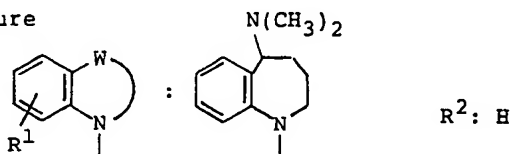
1-[4-(4-Dimethylaminobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline, colorless amorphous

$^1\text{H}$ -NMR (DMSO- $d_6$ )  $\delta$  : 1.90-2.00 (2H, m), 2.82 (2H, t,  $J=6.5$  Hz), 2.98 (6H, s), 3.77 (2H, t,  $J=6.5$  Hz), 6.70-7.30 (6H, m), 7.32 (2H, d,  $J=8.6$  Hz), 7.73 (2H, d,  $J=8.6$  Hz), 8.00-8.20 (1H, m), 8.39 (1H, d,  $J=2.2$  Hz), 10.37 (1H, s)

Using the suitable starting materials, the following compounds are obtained in the same manner as in Example 1.

Table 2

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**Example 406****Structure**

Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 216 - 218°C

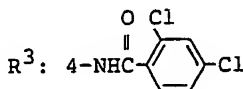
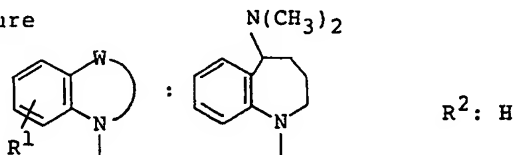
Form: Free

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Example 407

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

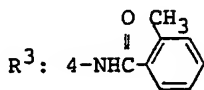
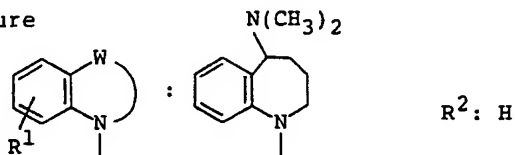
Melting Point: 181 - 183°C

Form: Free

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## Example 408

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 207 - 208°C

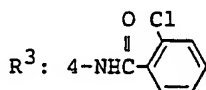
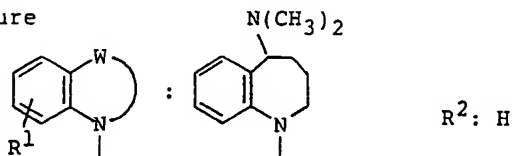
Form: Free

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Example 409

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

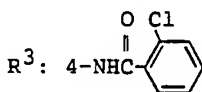
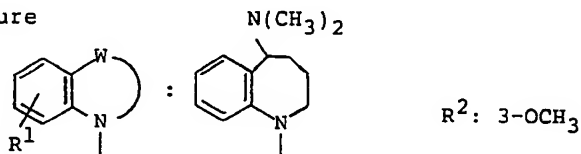
Melting Point: 213 - 214°C

Form: Free

---

## Example 410

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 136 - 138°C

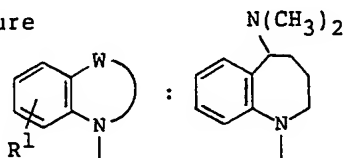
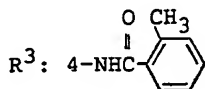
Form: Free

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Example 411

Structure

 $R^2: 3-OCH_3$ 

Crystalline form: White powder

Recrystallization solvent: Ethanol

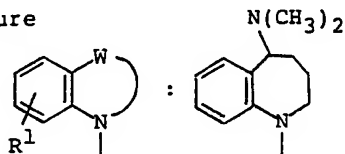
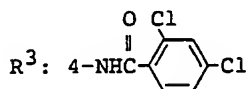
Melting Point: 130 - 132°C

Form: Free

---

## Example 412

Structure

 $R^2: 3-OCH_3$ 

Crystalline form: White powder

Recrystallization solvent: Ethanol

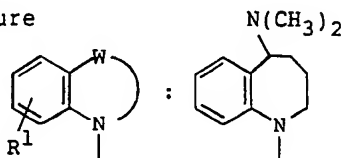
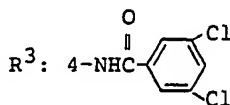
Melting Point: 143 - 145°C

Form: Free

---

## Example 413

Structure

 $R^2: 3\text{-OCH}_3$ 

Crystalline form: White powder

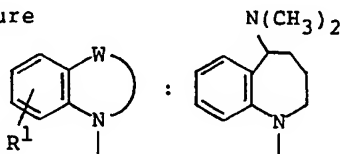
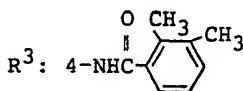
Recrystallization solvent: Ethanol

Melting Point: 171 - 173°C

Form: Free

## Example 414

Structure

 $R^2: 3\text{-OCH}_3$ 

Crystalline form: White powder

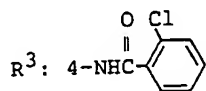
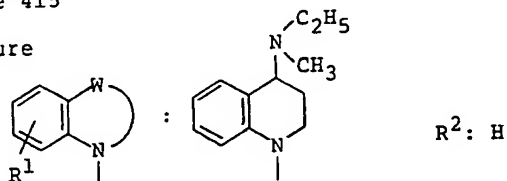
Recrystallization solvent: Ethanol

Melting Point: 162 - 164°C

Form: Free

## Example 415

Structure



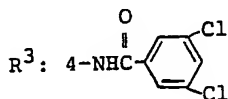
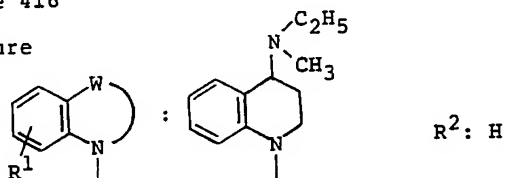
Crystalline form: Colorless amorphous

NMR analysis: 49)

Form: Free

## Example 416

Structure



Crystalline form: Colorless amorphous

NMR analysis: 50)

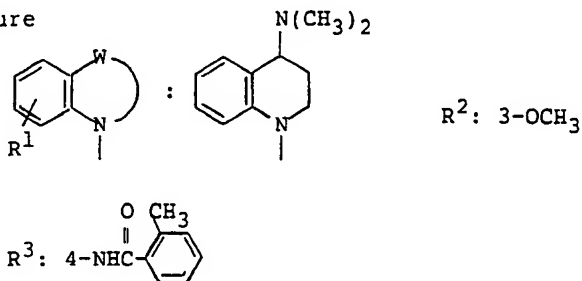
Form: Free



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Example 417

Structure



Crystalline form: Colorless amorphous

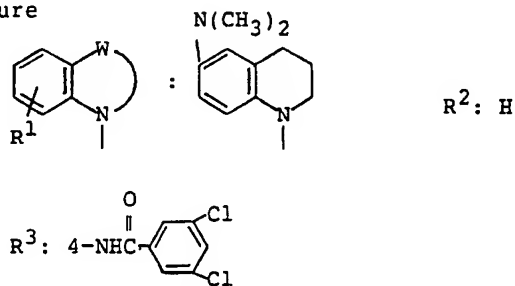
NMR analysis: 51)

Form: Free

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Example 418

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 228.5 - 230°C

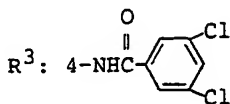
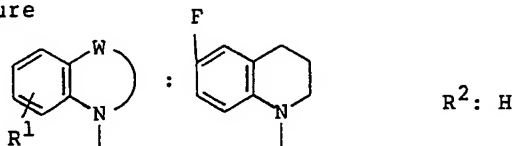
Form: Free

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Example 419

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

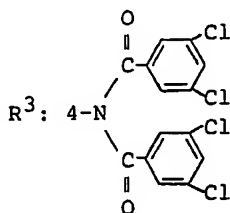
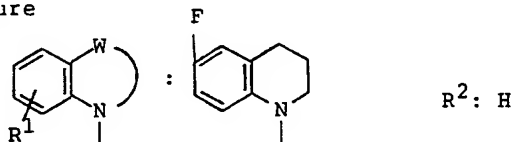
Melting Point: 205.5 - 206.5°C

Form: Free

---

## Example 420

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 210 - 212°C

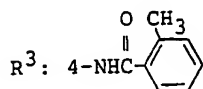
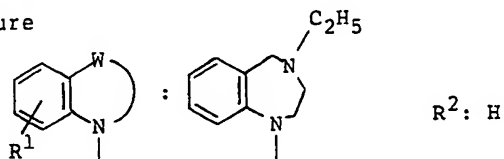
Form: Free

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Example 421

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

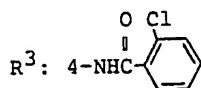
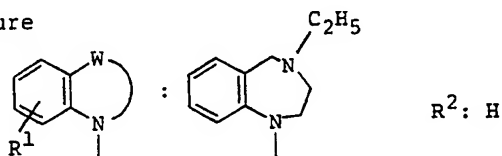
Melting Point: 166 - 167°C

Form: Free

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## Example 422

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 191.5 - 192.5°C

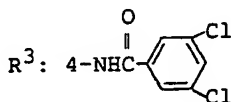
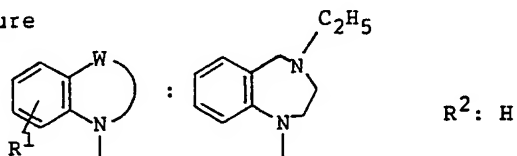
Form: Free

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Example 423

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

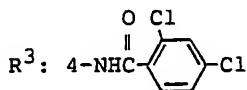
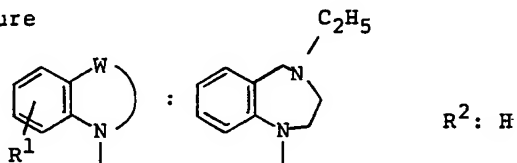
Melting Point: 209 - 210°C

Form: Free

---

## Example 424

Structure



Crystalline form: Colorless amorphous

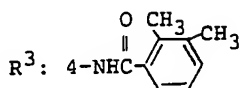
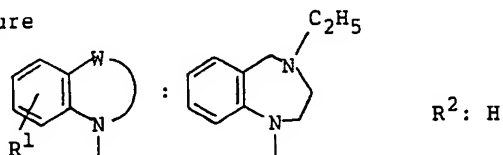
NMR analysis: 52)

Form: Free

---

## Example 425

Structure



Crystalline form: White powder

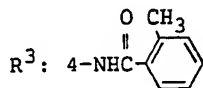
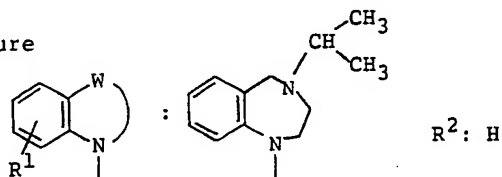
Recrystallization solvent: Ethanol

Melting Point: 148 - 149°C

Form: Free

## Example 426

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

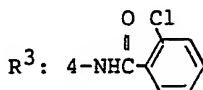
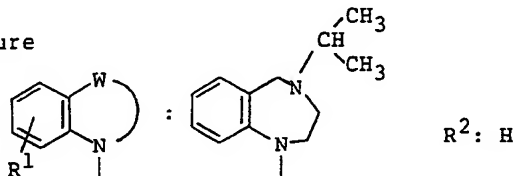
Melting Point: 157 - 158°C

Form: Free

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Example 427

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

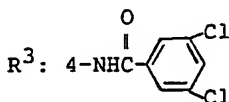
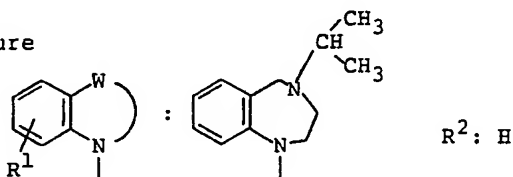
Melting Point: 194.5 - 195.5°C

Form: Free

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Example 1428

Structure



Crystalline form: White powder

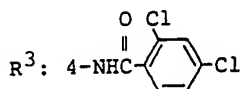
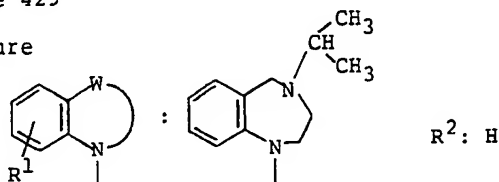
Recrystallization solvent: Ethanol

Melting Point: 179.5 - 180.5°C

Form: Free

## Example 429

Structure



Crystalline form: White powder

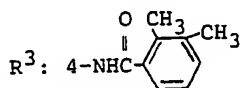
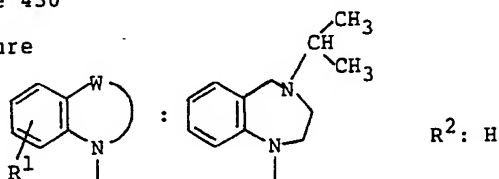
Recrystallization solvent: Ethanol

Melting Point: 190 - 191°C

Form: Free

## Example 430

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

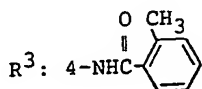
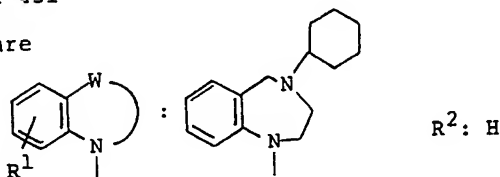
Melting Point: 159 - 160°C

Form: Free

---

Example 431

Structure



Crystalline form: Colorless amorphous

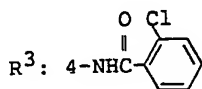
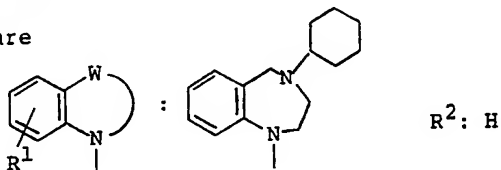
NMR analysis: 53)

Form: Hydrochloride

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## Example 432

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 155 - 156°C

Form: Free

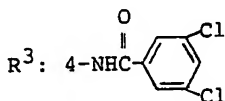
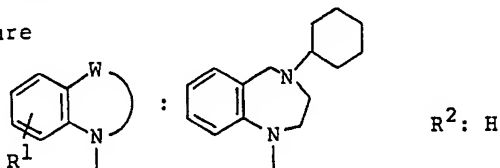
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Example 433

Structure



Crystalline form: Colorless amorphous

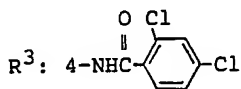
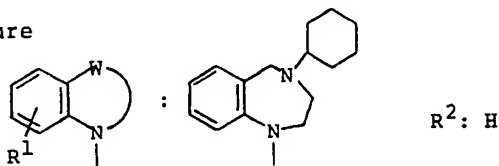
NMR analysis: 54)

Form: Free

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## Example 434

Structure



Crystalline form: Colorless amorphous

NMR analysis: 55)

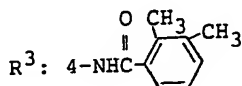
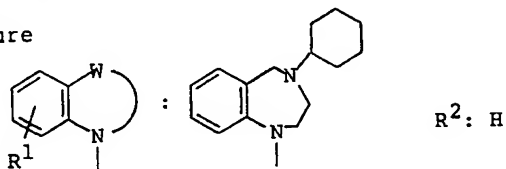
Form: Free

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Example 435

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

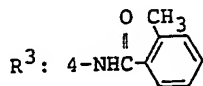
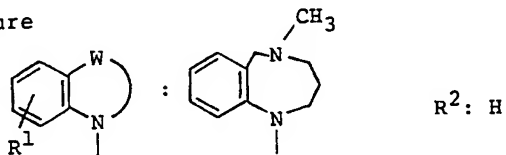
Melting Point: 175 - 177°C

Form: Free

---

## Example 436

Structure



Crystalline form: Colorless amorphous .

NMR analysis: 56)

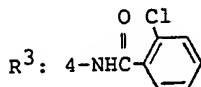
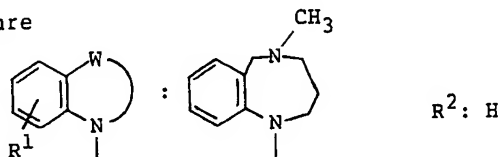
Form: Free

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Example 437

Structure



Crystalline form: Colorless amorphous

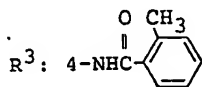
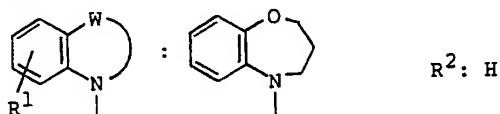
NMR analysis: 57)

Form: Free

---

## Example 438

Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

Melting Point: 219 - 220°C

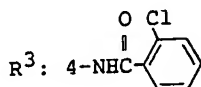
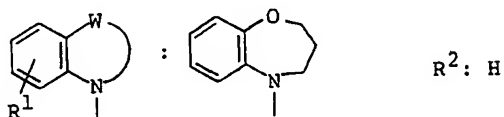
Form: Free

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Example 439

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/diethyl ether

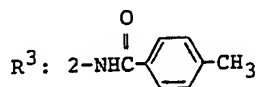
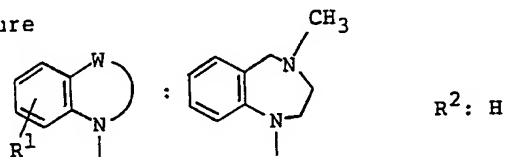
Melting Point: 215 - 218°C

Form: Free

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## Example 440

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 128.5 - 129.5°C

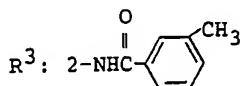
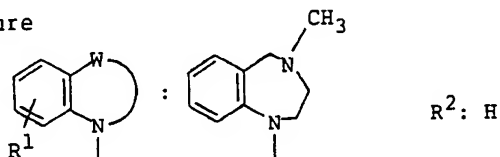
Form: Free

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Example 441

Structure



Crystalline form: Colorless amorphous

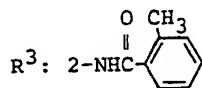
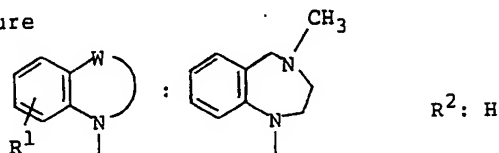
NMR analysis: 58)

Form: Free

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## Example 442

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 153 - 154°C

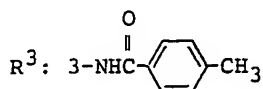
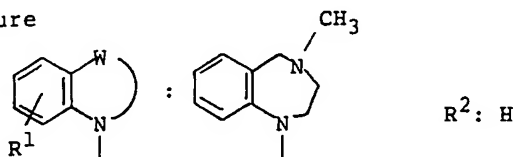
Form: Free

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Example 443

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

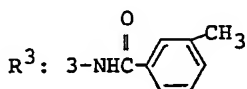
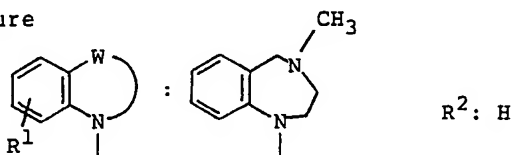
Melting Point: 150 - 153°C

Form: Free

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## Example 444

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 139 - 141°C

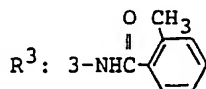
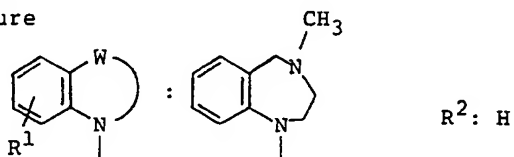
Form: Free

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Example 445

Structure



Crystalline form: Colorless amorphous

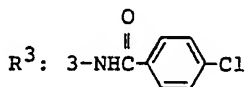
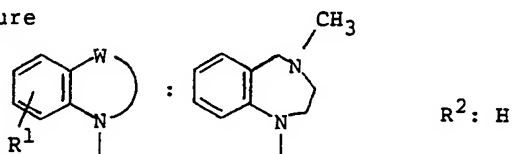
NMR analysis: 59)

Form: Free

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## Example 446

Structure



Crystalline form: Colorless amorphous

NMR analysis: 60)

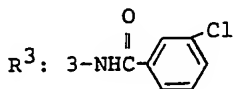
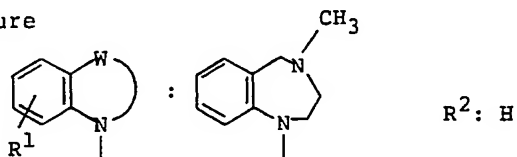
Form: Free

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Example 447

Structure



Crystalline form: Colorless amorphous

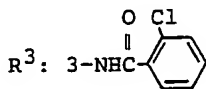
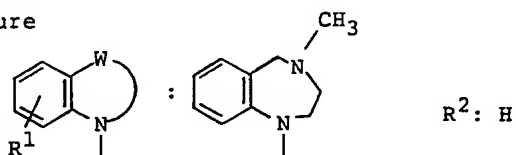
NMR analysis: 61)

Form: Free

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## Example 448

Structure



Crystalline form: Colorless amorphous

NMR analysis: 62)

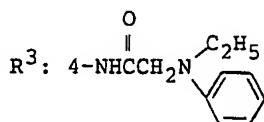
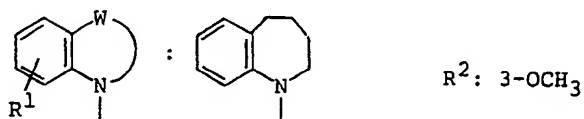
Form: Free

---



## Example 449

## Structure



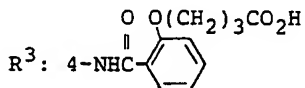
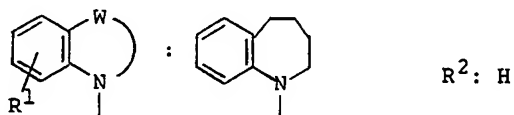
Crystalline form: Colorless amorphous

NMR analysis: 63)

Form: Free

## Example 450

## Structure



Crystalline form: White powder

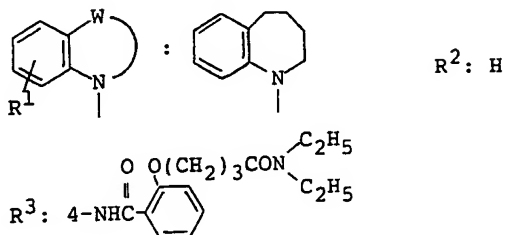
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 172.5 - 173.5°C

Form: Free

## Example 451

## Structure



Crystalline form: Colorless prisms

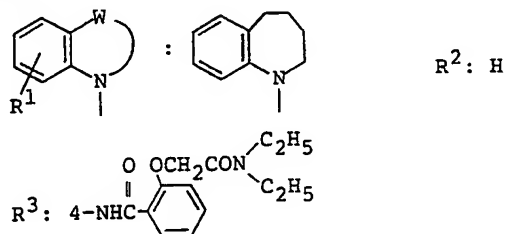
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 122.5 - 123°C

Form: Free

## Example 452

## Structure



Crystalline form: White powder

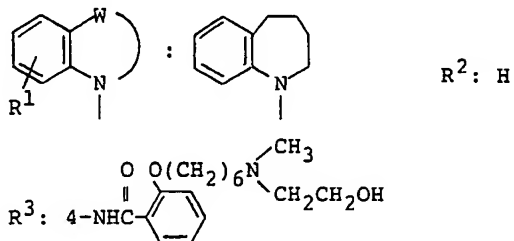
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 198 - 199.5°C

Form: Free

## Example 453

## Structure



Crystalline form: White powder

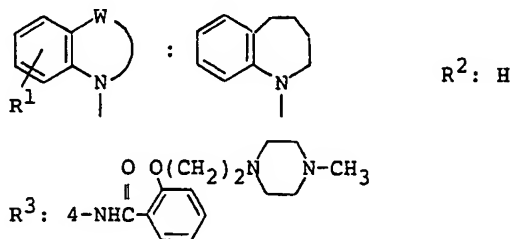
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 118 - 119.5°C

Form: Hydrochloride

## Example 454

## Structure



Crystalline form: White powder

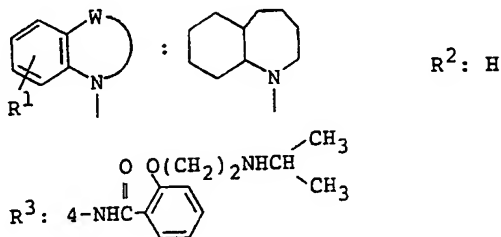
Recrystallization solvent: Ethanol

Melting Point: 163 - 165°C

Form: Dihydrochloride

## Example 455

## Structure



Crystalline form: White powder

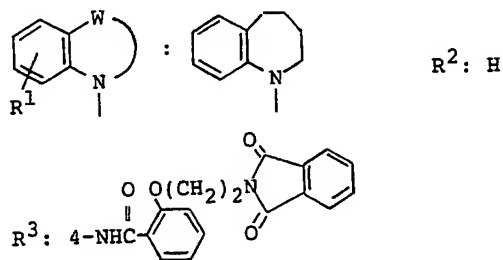
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 246 - 248°C

Form: Hydrochloride

## Example 456

## Structure



Crystalline form: White powder

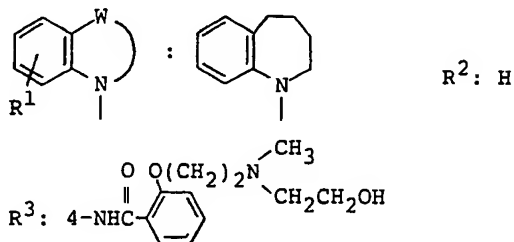
Recrystallization solvent: Chloroform/ethanol

Melting Point: 204 - 205°C

Form: Free

## Example 457

## Structure



Crystalline form: Colorless prisms

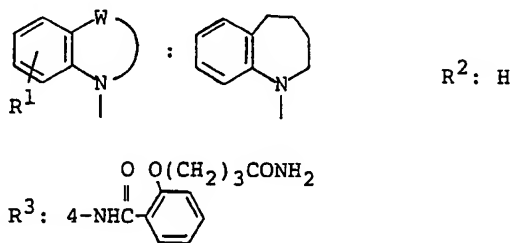
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 127 - 128°C

Form: Hydrochloride

## Example 458

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

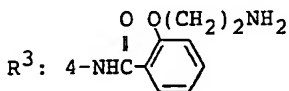
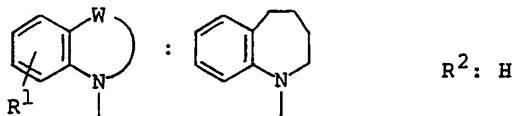
Melting Point: 220 - 221°C

Form: Free

---

Example 459

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

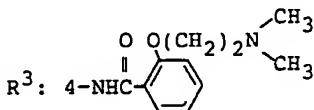
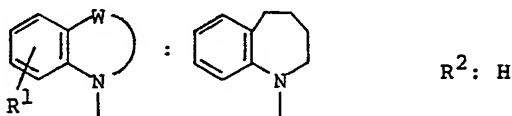
Melting Point: 190 - 192°C

Form: Free

---

## Example 460

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 189 - 191°C

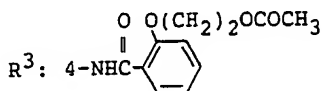
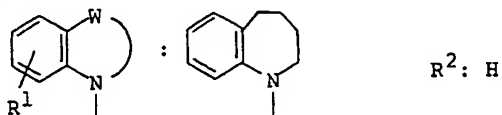
Form: Hydrochloride

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Example 461

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

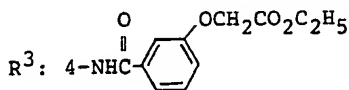
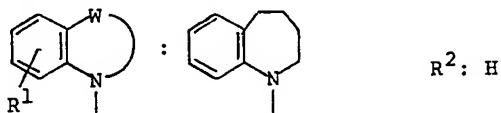
Melting Point: 173 - 174°C

Form: Free

---

## Example 462

## Structure



Crystalline form: White powder

Recrystallization solvent: Dichloromethane/ethanol

Melting Point: 129 - 130°C

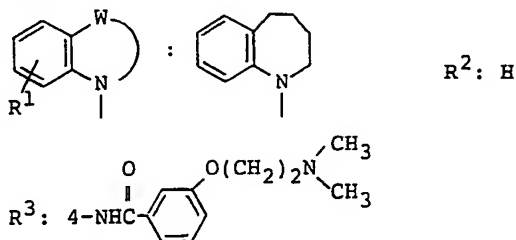
Form: Free

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---

Example 463

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

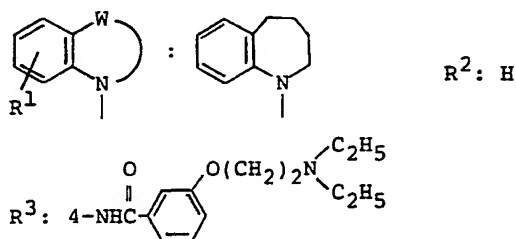
Melting Point: 130 - 133°C

Form: Hydrochloride

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## Example 464

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 170.5 - 172°C

Form: Hydrochloride

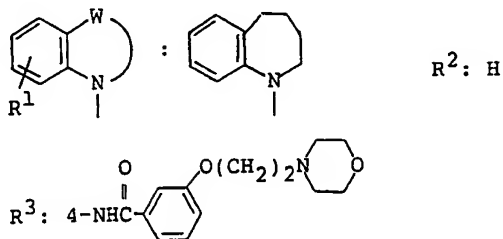
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Example 465

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

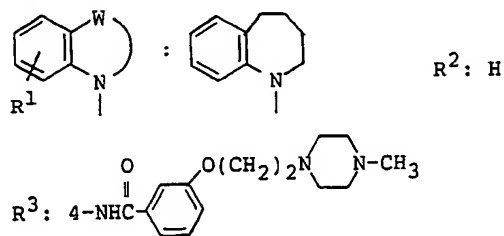
Melting Point: 126 - 131°C

Form: Hydrochloride

---

## Example 466

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 182 - 185°C

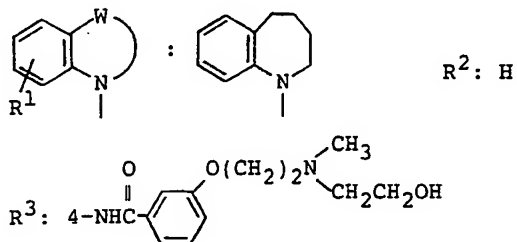
Form: Dihydrochloride

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Example 467

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

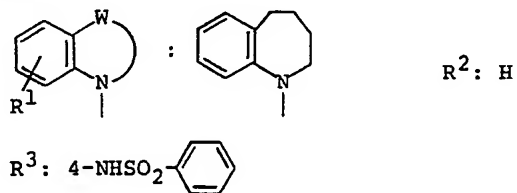
Melting Point: 116 - 121°C

Form: Hydrochloride

---

## Example 468

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 178 - 182.5°C

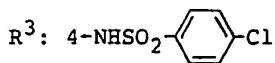
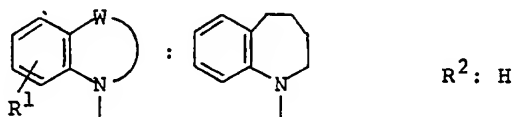
Form: Free

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Example 469

## Structure



Crystalline form: Colorless particles

Recrystallization solvent: Methanol/diethyl ether

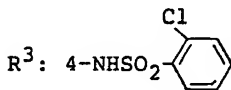
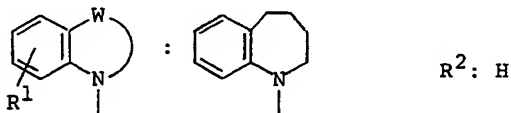
Melting Point: 185 - 187°C

Form: Free

---

## Example 470

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 215 - 217°C

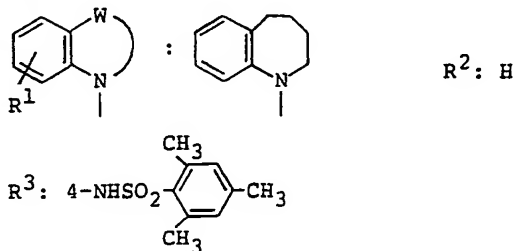
Form: Free

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Example 471

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

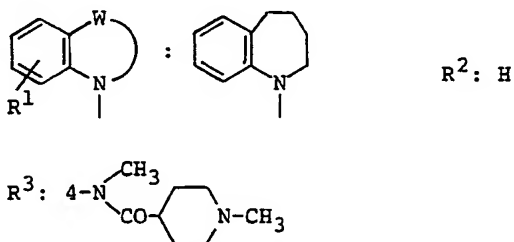
Melting Point: 176 - 178°C

Form: Free

---

## Example 472

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Methanol/n-hexane

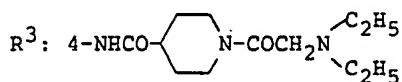
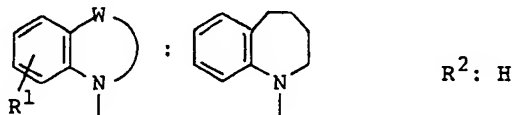
Melting Point: 194.5 - 197°C

Form: Free

---

## Example 473

## Structure



Crystalline form: White powder

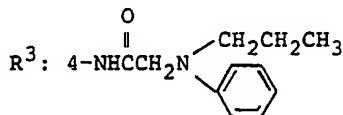
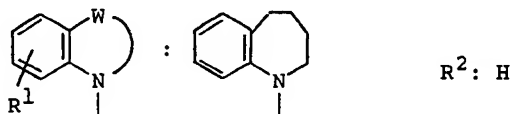
Recrystallization solvent: Methanol/diethyl ether

Melting Point: 161.5 - 165.5°C

Form: Hydrochloride

## Example 474

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

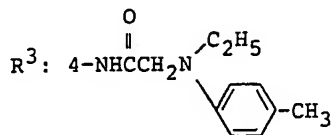
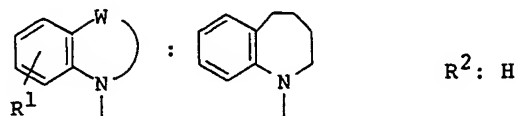
Melting Point: 152 - 153°C

Form: Free

---

Example 475

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: n-Hexane/ethyl acetate

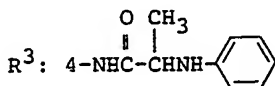
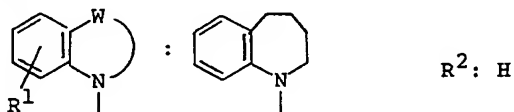
Melting Point: 147 - 148°C

Form: Free

---

## Example 476

## Structure



Crystalline form: Light yellow powder

Recrystallization solvent: Ethyl acetate

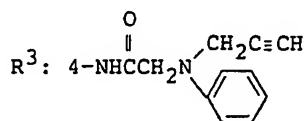
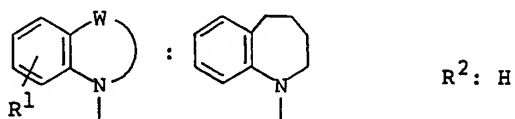
Melting Point: 215 - 217°C

Form: Free

---

## Example 477

## Structure



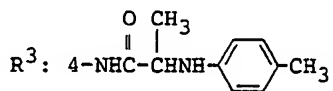
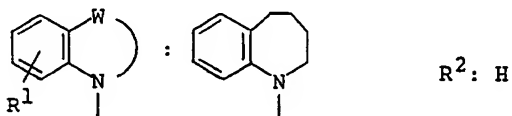
Crystalline form: Colorless amorphous

NMR analysis: 64)

Form: Free

## Example 478

## Structure



Crystalline form: White powder

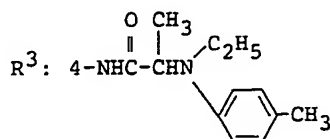
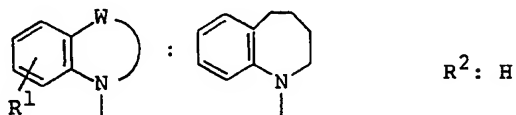
Recrystallization solvent: Ethyl acetate

Melting Point: 180 - 181°C

Form: Free

## Example 479

## Structure



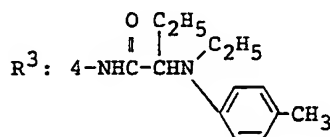
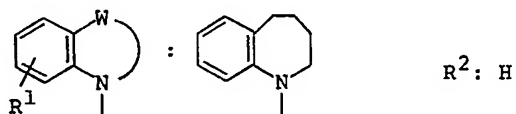
Crystalline form: Colorless amorphous

NMR analysis: 65)

Form: Free

## Example 480

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 66)

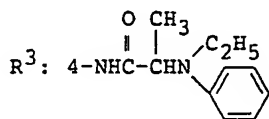
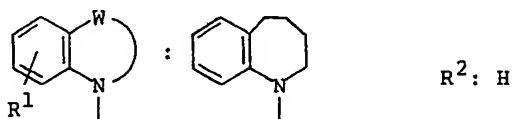
Form: Free



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Example 481

## Structure



Crystalline form: Colorless amorphous .

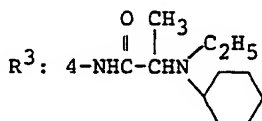
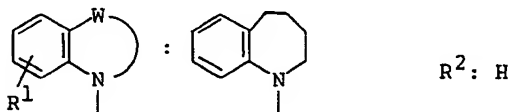
NMR analysis: 67)

Form: Free

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Example 482

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 165 - 167°C

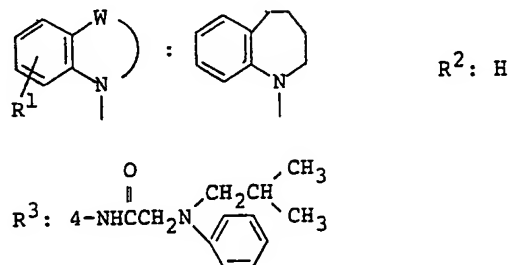
Form: Free

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Example 483

## Structure



Crystalline form: Colorless amorphous

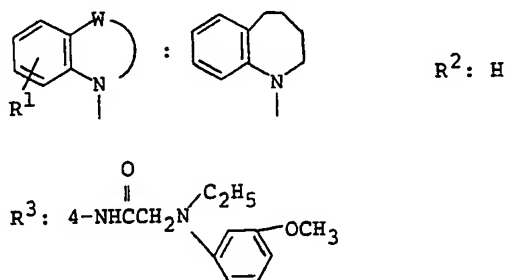
NMR analysis: 68)

Form: Free

---

Example 484

## Structure



Crystalline form: Colorless amorphous

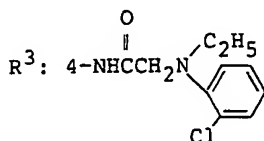
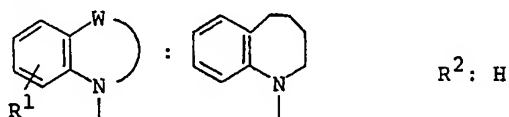
NMR analysis: 69)

Form: Free

---

Example 485

## Structure



Crystalline form: Colorless amorphous

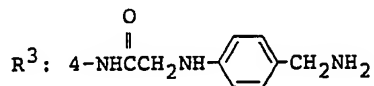
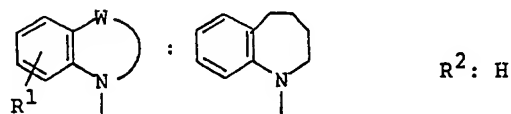
NMR analysis: 70)

Form: Free

---

Example 486

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 71)

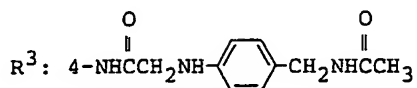
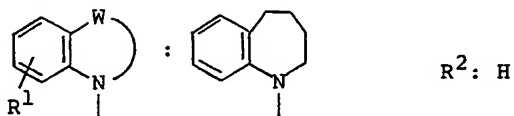
Form: Free

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Example 487

## Structure



Crystalline form: Colorless amorphous

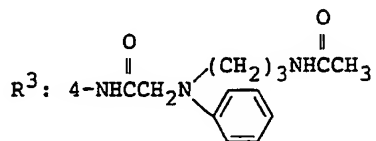
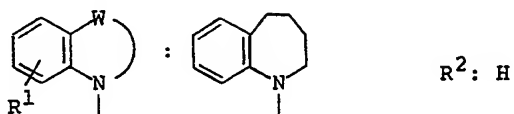
NMR analysis: 72)

Form: Free

---

## Example 488

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 73)

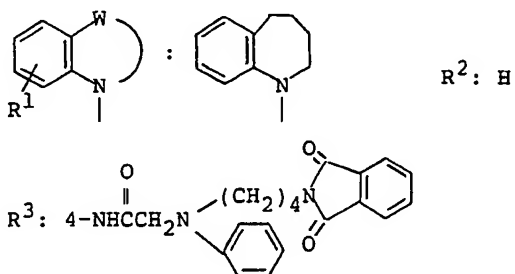
Form: Free

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Example 489

## Structure



Crystalline form: Light yellow amorphous

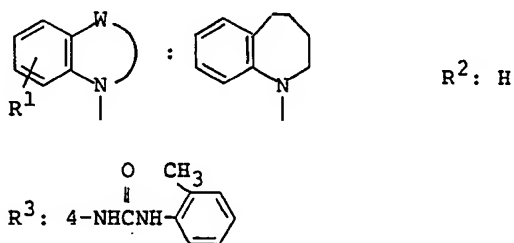
NMR analysis: 74)

Form: Free

---

Example 490

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

Melting Point: 182 - 182.5°C

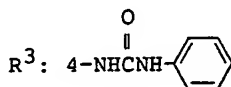
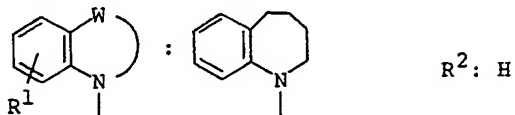
Form: Free

---

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Example 491

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

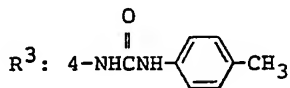
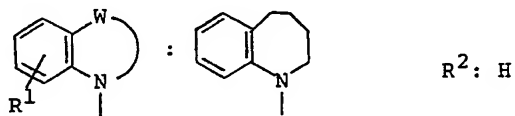
Melting Point: 244 - 245°C

Form: Free

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## Example 492

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

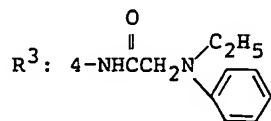
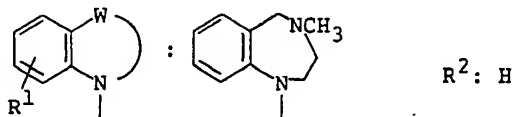
Melting Point: 220 - 221.5°C

Form: Free

---

## Example 493

## Structure



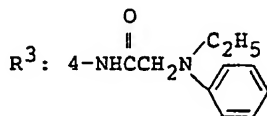
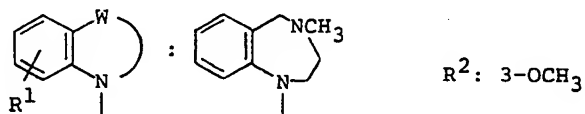
Crystalline form: Light yellow amorphous

NMR analysis: 75)

Form: Free

## Example 494

## Structure



Crystalline form: Light yellow amorphous

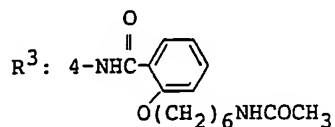
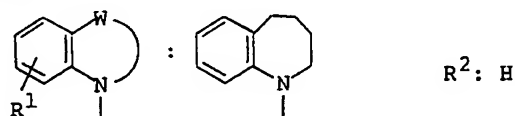
NMR analysis: 76)

Form: Free

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Example 495

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Methanol/diethyl ether

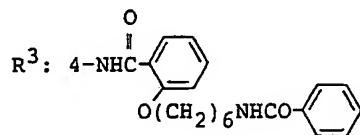
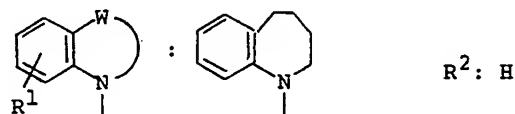
Melting Point: 171 - 172°C

Form: Free

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## Example 496

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 178 - 178.5°C

Form: Free

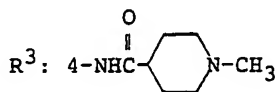
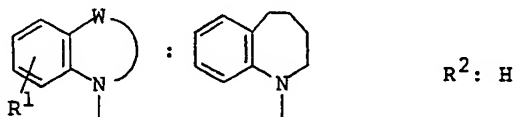
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 Example 497

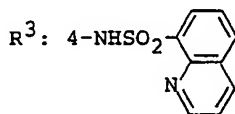
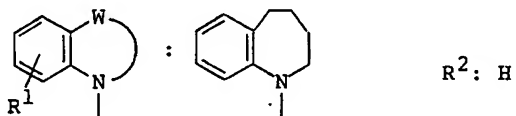
## Structure




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 Example 498

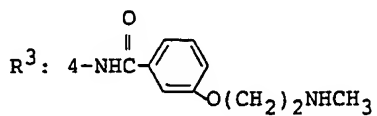
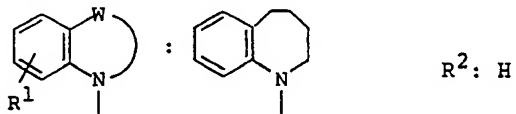
## Structure




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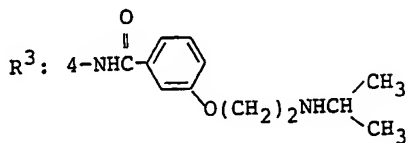
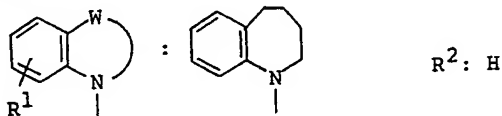
 Example 499

## Structure



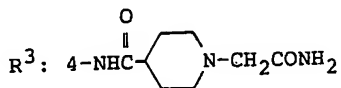
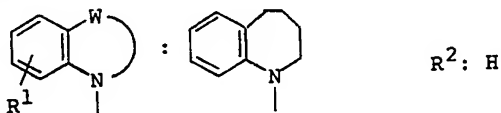
## Example 500

## Structure



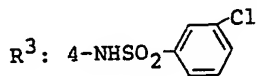
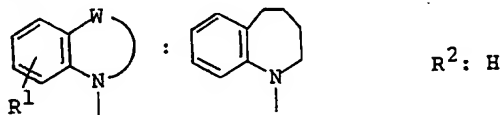
## Example 501

## Structure



## Example 502

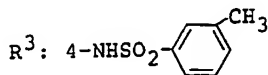
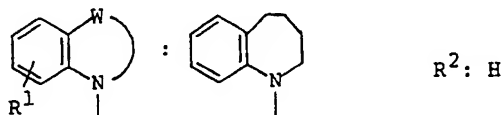
## Structure



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Example 503

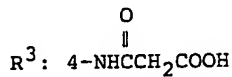
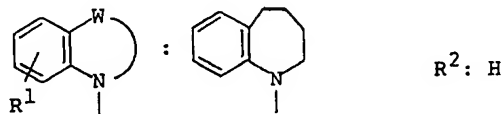
## Structure



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Example 504

## Structure



Crystalline form: Light yellow scales

Recrystallization solvent: Ethanol/water

Melting Point: 129 - 131°C

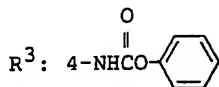
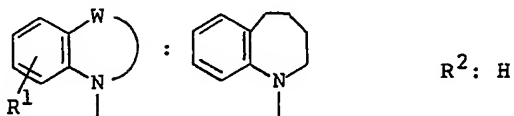
Form: Free

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Example 505

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate

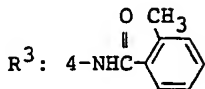
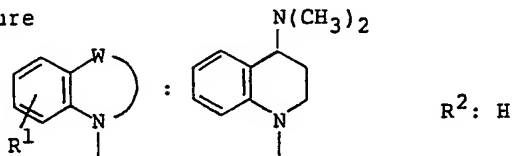
Melting Point: 199 - 201°C

Form: Free

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## Example 506

## Structure



Crystalline form: Colorless amorphous

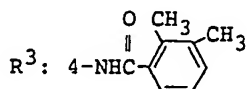
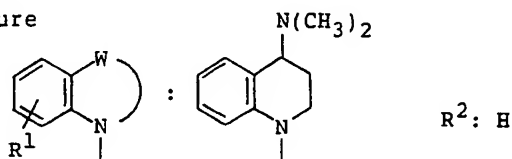
NMR analysis: 77)

Form: Free

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## Example 507

Structure



Crystalline form: White powder

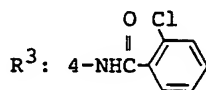
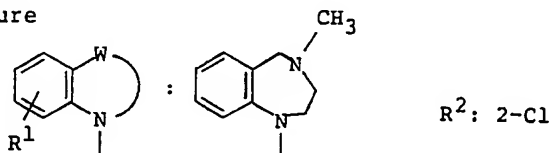
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 187.5 - 189°C

Form: Free

## Example 508

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

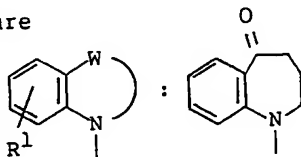
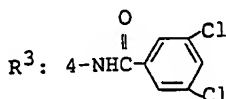
Melting Point: 161 - 164°C

Form: Free

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Example 509

Structure

 $R^2$ : H

Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

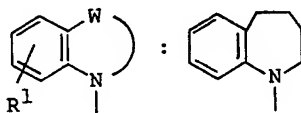
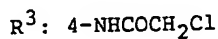
Melting Point: 242 - 243°C

Form: Free

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## Example 510

Structure

 $R^2$ : 3-OCH<sub>3</sub>

Crystalline form: White powder

Recrystallization solvent: Dichloroethane/diethyl ether

Melting Point: 186 - 188°C

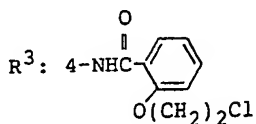
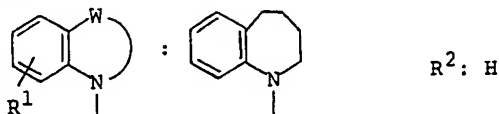
Form: Free

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Example 511

## Structure



Crystalline form: Colorless amorphous

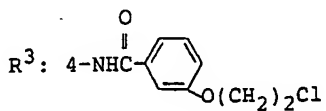
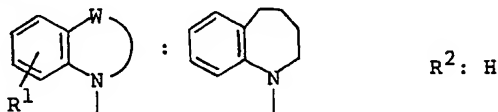
NMR analysis: 78)

Form: Free

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## Example 512

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 79)

Form: Free

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- 49)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.11 (3H, t,  $J=7.1$  Hz), 1.90-2.25 (2H, m), 2.29 (3H, s), 2.55 (2H, q,  $J=7.1$  Hz), 3.62-3.90 (2H, m), 4.00-4.20 (1H, m), 6.63 (1H, d,  $J=7.9$  Hz), 6.85-7.10 (2H, m), 7.25-7.80 (9H, m), 8.25 (1H, brs)
- 50)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.10 (3H, t,  $J=7.1$  Hz), 1.90-2.20 (2H, m), 2.28 (3H, s), 3.60-3.90 (2H, m), 3.95-4.20 (1H, m), 6.62 (1H, d,  $J=7.9$  Hz), 6.80-7.10 (2H, m), 7.20 (2H, d,  $J=8.6$  Hz), 7.31-7.55 (4H, m), 7.80 (2H, d,  $J=1.9$  Hz), 9.05 (1H, brs)
- 51)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.80-2.05 (1H, m), 2.15-2.50 (1H, m), 2.34 (6H, s), 2.51 (3H, s), 3.48-3.62 (1H, m), 3.72 (3H, s), 3.70-3.85 (1H, m), 4.00-4.22 (1H, m), 6.64 (1H, d,  $J=7.8$  Hz), 6.84-7.58 (9H, m), 8.16 (1H, brs), 8.40 (1H, d,  $J=8.7$  Hz)
- 52)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.16 (3H, t,  $J=7.1$  Hz), 2.40-2.70 (2H, m), 2.90-3.30 (3H, m), 3.80-4.20 (2H, m), 4.80-5.00 (1H, m), 6.60-6.80 (1H, m), 7.00-7.70 (10H, m), 8.24 (1H, s)
- 53)  $^1\text{H-NMR}(\text{DMSO}-d_6)$   $\delta$  ; 1.0-2.5 (10H, m), 2.34 (3H, s), 3.30-3.80 (4H, m), 4.50-5.30 (3H, m), 6.70-7.00 (1H, m), 7.10-7.80 (11H, m), 10.43 (1H, s), 10.5-12.0 (1H, br)
- 54)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.10-2.10 (10H, m), 2.40-2.70 (1H, m), 2.80-3.20 (3H, m), 3.92 (2H, s), 4.90-5.20 (1H, m), 6.50-6.70 (1H, m), 6.80-7.60 (8H, m), 7.75



- (2H, s), 8.73 (1H, s)
- 55)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.10-2.20 (10H, m), 2.40-2.70 (1H, m), 2.90-3.30 (3H, m), 3.93 (2H, s), 4.90-5.20 (1H, m), 6.62 (1H, d,  $J=7.6$  Hz), 6.90-7.70 (10H, m), 8.29 (1H, s)
- 56)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.50-2.10 (2H, m), 2.38 (6H, s), 2.30-2.70 (1H, m), 2.70-3.00 (2H, m), 3.45 (1H, d,  $J=13$  Hz), 3.81 (1H, d,  $J=14$  Hz), 4.70-5.00 (1H, m), 7.0-7.50 (12H, m), 8.23 (1H, s)
- 57)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.50-2.10 (2H, m), 2.42 (3H, s), 2.40-2.70 (1H, m), 2.80-3.00 (2H, m), 3.52 (1H, d,  $J=13$  Hz), 3.85 (1H, d,  $J=13$  Hz), 4.70-5.00 (1H, m), 7.00-7.70 (12H, m), 8.54 (1H, s)
- 58)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.43 (3H, s), 2.47 (3H, s), 3.00-3.30 (3H, m), 3.76 (1H, d,  $J=14$  Hz), 4.06 (1H, d,  $J=14$  Hz), 4.90-5.20 (1H, m), 6.50-6.80 (3H, m), 6.90-7.50 (6H, m), 7.70-8.00 (2H, m), 8.48 (1H, d,  $J=8$  Hz), 10.58 (1H, s)
- 59)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.41 (3H, s), 2.44 (3H, s), 2.90-3.20 (3H, m), 3.74 (1H, d,  $J=13$  Hz), 4.07 (1H, d,  $J=14$  Hz), 4.80-5.00 (1H, m), 6.67 (1H, d,  $J=7$  Hz), 6.76 (1H, d,  $J=7$  Hz), 7.00-7.50 (8H, m), 7.55 (1H, s), 7.70-7.90 (2H, m)
- 60)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.41 (3H, s), 2.80-3.20 (3H, m), 3.73 (1H, d,  $J=13$  Hz), 4.03 (1H, d,  $J=14$  Hz), 6.66 (2H, d,  $J=7.6$  Hz), 6.90-8.00 (10H, m), 8.57 (1H, s)

- 61)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.40 (3H, s), 2.90-3.20 (3H, m), 3.73 (1H, d,  $J=13$  Hz), 4.07 (1H, d,  $J=13$  Hz), 4.70-5.00 (1H, m), 6.60-6.80 (2H, m), 6.90-8.00 (10H, m), 8.54 (1H, s)
- 62)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.41 (3H, s), 2.90-3.20 (3H, m), 3.75 (1H, d,  $J=14$  Hz), 4.08 (1H, d,  $J=14$  Hz), 4.80-5.00 (1H, m), 6.67 (1H, d,  $J=7.6$  Hz), 6.82 (1H, d,  $J=7.6$  Hz), 6.90-7.90 (10H, m), 8.08 (1H, s)
- 63)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.23 (3H, t,  $J=7$  Hz), 1.40-1.70 (1H, m), 1.90-2.20 (3H, m), 2.70-3.30 (3H, m), 3.40-3.60 (5H, m), 3.91 (2H, s), 5.00-5.20 (1H, m), 6.60-7.40 (11H, m), 8.12 (1H, d,  $J=8$  Hz), 8.99 (1H, s)
- 64)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.35-1.70 (1H, m), 1.80-2.20 (3H, m), 2.25-2.35 (1H, m), 2.65-3.20 (3H, m), 4.01 (2H, s), 4.05-4.17 (2H, m), 4.90-5.10 (1H, m), 6.61 (1H, d,  $J=7.5$  Hz), 6.75-7.50 (12H, m), 8.44 (1H, brs)
- 65)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.13 (3H, t,  $J=7.0$  Hz), 1.30-1.65 (4H, m), 1.80-2.20 (3H, m), 2.28 (3H, s), 2.65-3.40 (5H, m), 4.90-5.10 (1H, m), 6.63 (1H, d,  $J=7.8$  Hz), 6.75-7.00 (3H, m), 7.00-7.45 (8H, m), 8.85 (1H, brs)
- 66)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 0.88 (3H, t,  $J=7.4$  Hz), 1.16 (3H, t,  $J=7.0$  Hz), 1.35-2.20 (6H, m), 2.27 (3H, s), 2.60-3.20 (3H, m), 3.20-3.45 (2H, m), 3.85-4.10 (1H, m), 4.90-5.10 (1H, m), 6.63 (1H, d,  $J=7.4$  Hz),

- 6.77 (2H, d, J=8.5 Hz), 6.92 (1H, t, J=8.0 Hz),  
7.00-7.45 (8H, m), 8.85 (1H, brs)
- 67)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.17 (3H, t, J=7.0 Hz), 1.35-1.65  
(4H, m), 2.60-3.45 (5H, m), 4.20 (2H, q, J=7.0 Hz),  
4.90-5.10 (1H, m), 6.63 (1H, d, J=7.6 Hz), 6.80-  
7.45 (12H, m), 8.66 (1H, brs)
- 68)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 0.96 (6H, d, J=6.6 Hz), 1.35-1.65  
(1H, m), 1.80-2.25 (4H, m), 2.65-3.15 (3H, m), 3.19  
(2H, d, J=7.3 Hz), 3.99 (2H, s), 4.90-5.10 (1H, m),  
6.60 (1H, d, J=7.8 Hz), 6.75-7.05 (4H, m), 7.05-  
7.40 (8H, m), 8.15 (1H, brs)
- 69)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.19 (3H, t, J=7.0 Hz), 1.35-1.65  
(1H, m), 1.80-2.25 (3H, m), 2.70-3.20 (3H, m), 3.44  
(2H, q, J=7.0 Hz), 3.77 (3H, s), 3.87 (2H, s),  
4.90-5.10 (1H, m), 6.25-6.50 (3H, m), 6.67 (1H, d,  
J=7.5 Hz), 6.85-7.45 (8H, m), 8.29 (1H, brs)
- 70)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.05 (3H, t, J=7.1 Hz), 1.35-1.65  
(1H, m), 1.85-2.25 (3H, m), 2.65-3.30 (5H, m), 3.74  
(2H, s), 4.95-5.15 (1H, m), 6.63 (1H, d, J=7.5 Hz),  
6.80-7.55 (11H, m), 9.51 (1H, brs)
- 71)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.30-1.65 (1H, m), 1.80-2.30 (3H,  
m), 2.65-3.15 (3H, m), 3.75 (2H, s), 3.74 (2H, s),  
4.95-5.10 (1H, m), 6.45-6.70 (3H, m), 6.88 (1H, t,  
J=6.8 Hz), 7.00-7.45 (8H, m), 8.74 (1H, brs)
- 72)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.30-1.70 (1H, m), 1.75-2.25 (6H,  
m), 2.65-3.15 (3H, m), 3.78 (2H, d, J=5.4 Hz), 4.28

- (2H, d,  $J=5.5$  Hz), 4.53 (1H, brs), 4.90-5.10 (1H, m), 5.89 (1H, brs), 6.50-6.70 (3H, m), 6.89 (1H, t,  $J=7.5$  Hz), 7.00-7.40 (8H, m), 8.61 (1H, brs)
- 73)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.35-1.65 (1H, m), 1.70-2.20 (8H, m), 2.65-3.20 (3H, m), 3.25-3.55 (4H, m), 3.88 (2H, s), 4.90-5.10 (1H, m), 5.79 (1H, brs), 6.55-7.40 (13H, m), 8.37 (1H, brs)
- 74)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.35-2.00 (8H, m), 2.65-3.20 (3H, m), 3.30-3.35 (2H, m), 3.60-3.85 (2H, m), 3.90 (2H, s), 4.95-5.15 (1H, m), 6.55-7.00 (5H, m), 7.00-7.40 (8H, m), 7.65-7.90 (4H, m), 8.22 (1H, brs)
- 75)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.16 (3H, t,  $J=7.0$  Hz), 2.39 (3H, s), 2.80-3.20 (3H, m), 3.44 (2H, q,  $J=7.0$  Hz), 3.65-4.20 (4H, m), 4.80-5.05 (1H, m), 6.50-7.45 (13H, m), 8.50 (1H, brs)
- 76)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.23 (3H, t,  $J=7.0$  Hz), 2.41 (3H, s), 2.75-3.20 (3H, m), 3.40-3.60 (5H, m), 3.65-3.90 (1H, m), 3.92 (2H, s), 3.90-4.20 (1H, m), 4.85-5.10 (1H, m), 6.65-7.45 (11H, m), 8.13 (1H, d,  $J=8.4$  Hz), 9.01 (1H, brs)
- 77)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.80-1.95 (1H, m), 2.20-2.70 (10H, m), 3.50-3.60 (1H, m), 3.63-3.80 (1H, m), 4.00-4.15 (1H, m), 6.60 (1H, d,  $J=7.6$  Hz), 6.92 (1H, t,  $J=7.6$  Hz), 7.02 (1H, t,  $J=6.3$  Hz), 7.20-7.65 (9H, m), 7.87 (1H, brs)
- 78)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.40-1.62 (1H, m), 1.84-2.22 (3H,

m), 2.65-3.19 (3H, m), 3.97 (2H, t, J=4.9 Hz), 4.43 (2H, t, J=4.9 Hz), 4.95-5.18 (1H, m), 6.60-6.77 (1H, m), 6.85-7.02 (2H, m), 7.02-7.30 (5H, m), 7.40-7.68 (3H, m), 8.20-8.32 (1H, m), 9.62-9.81 (1H, m)

79)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.38-1.65 (1H, m), 1.84-2.21 (3H, m), 2.64-3.15 (3H, m), 3.81 (2H, t, J=5.7 Hz), 4.25 (2H, t, J=5.7 Hz), 4.90-5.13 (1H, m), 6.58-6.71 (1H, m), 6.82-7.00 (1H, m), 7.00-7.52 (10H, m), 8.11 (1H, brs)

#### Example 513

To a solution of 1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (1.06 g) in dichloromethane (80 ml) is added o-methylphenyl isocyanate (0.66 g) under ice-cooling. The mixture is stirred at room temperature for 4 hours. After completion of the reaction, the solvent is concentrated under reduced pressure and the resulting residue is purified by silica gel column chromatography (eluent; n-hexane : ethyl acetate = 1 : 1), and recrystallized from ethyl acetate to give 1-[4-(2-methyl-anilinocarbonylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.97 g) as white powder, m.p. 182 - 182.5°C.

Using the suitable starting materials, the compounds of the above Examples 491 - 492 are obtained in the same manner as in Example 513.

#### Example 514

A mixture of 1-(4-aminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (0.50 g), phenylsulfonyl chloride (0.29 ml), triethylamine (0.32 ml) and dichloromethane (30 ml) is stirred at room temperature overnight. The reaction mixture is washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; chloroform), and recrystallized from methanol/diethyl ether to give 1-(4-phenylsulfonylaminobenzoyl)-2,3,4,5-tetrahydro-1H-benzazepine (0.27 g) as colorless prisms, m.p. 178 - 182.5°C.

Using the suitable starting materials, the compounds of the above Examples 469 - 471, 498, 502 and 503 are obtained in the same manner as in Example 514.

Example 515

To a solution of 1-[4-(4-piperidinylcarbonylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g) in dimethylformamide (20 ml) is added 60 % sodium hydride dispersion in mineral oil (82 mg) and the mixture is stirred at room temperature for 30 minutes. Thereto is added methyl iodide (0.14 ml) and the mixture is stirred at room temperature overnight. The solvent is distilled off and the resulting residue is extracted with chloroform, and washed successively with water and saturated saline solution, and dried over magnesium sulfate. The solvent is distilled off

and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 10 : 1), and recrystallized from methanol/n-hexane to give 1-{4-[N-(1-methyl-4-piperidinylcarbonyl)-N-methylamino]benzoyl}-2,3,4,5-tetrahydro-1H-benzazepine (0.03 g) as light yellow powder, m.p. 194.5 - 197°C.

Using the suitable starting materials, the compounds of the above Examples 497 and 501 are obtained in the same manner as in Example 515.

#### Example 516

6-Fluoro-1-(4-aminobenzoyl)-1,2,3,4-tetrahydroquinoline (0.15 g) is dissolved in dichloromethane (10 ml) and thereto is added triethylamine (0.31 ml). To the mixture is added dropwise a solution of 3,5-dichlorobenzoyl chloride (0.14 g) in dichloromethane (2.0 ml) under ice-cooling, and the mixture is stirred for 30 minutes under ice-cooling, and further, at room temperature for 1 hour. To the mixture are added triethylamine (0.31 ml) and 3,5-dichlorobenzoyl chloride (0.14 ml). The mixture is stirred at room temperature for 4 hours. The reaction mixture is washed with water, and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; ethyl acetate : n-hexane = 1 : 5 + 1 : 4), and recrystallized from ethyl acetate/n-hexane to give 6-fluoro-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-1,2,3,4-tetrahydroquinoline

(0.12 g) and 6-fluoro-1-(4-[bis-(3,5-dichlorobenzoyl)amino]-benzoyl)-1,2,3,4-tetrahydroquinoline.

The former: White powder, m.p. 205.5 - 206.5°C

The latter: White powder, m.p. 210.5 - 212°C

Example 517

Using the suitable starting materials, the compounds of the above Examples 450 and 504 are obtained in the same manner as in Example 378.

Example 518

Using the suitable starting materials, the compounds of the above Examples 450 - 467, 495, 496, 499, 500, 511 and 512 are obtained in the same manner as in Example 380.

Example 519

Using the suitable starting materials, the compounds of the above Examples 449, 474 - 489, 493 and 494 are obtained in the same manner as in Example 394.

Example 520

Using the suitable starting materials, the compounds of the above Examples 453, 455, 457, 459, 460, 463 - 467, 495, 496 and 499 are obtained in the same manner as in Example 397.

Example 521

Using the suitable starting materials, the compound of the above Example 461 is obtained in the same manner as



in Example 396.

Example 522

Using the suitable starting materials, the compound of the above Example 456 is obtained in the same manner as in Example 398.

Example 523

Using the suitable starting materials, the compound of the above Example 459 is obtained in the same manner as in Example 399.

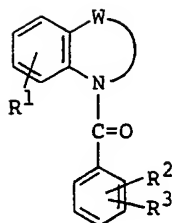
Example 524

Using the suitable starting materials, the compounds of the above Examples 495 and 496 are obtained in the same manner as in Examples 400 and 401.

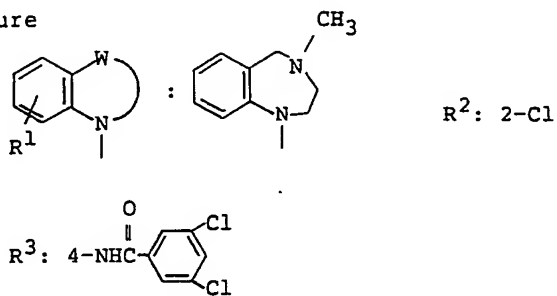
Example 525

Using the suitable starting materials, the compound of the above Example 458 is obtained in the same manner as in Example 402.

Using the suitable starting materials, the compounds of the following Table 3 are obtained in the same manner as in Examples 1 and 382.

Table 3

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**Example 527****Structure**

Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 225 - 226°C

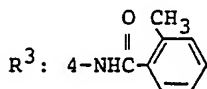
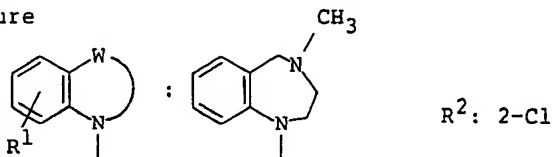
Form: Free

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Example 528

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

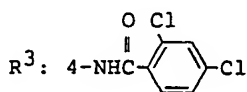
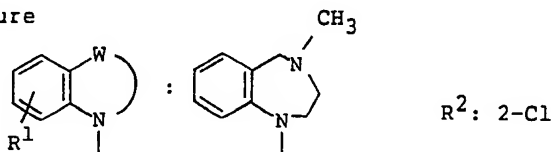
Melting Point: 142.5 - 145°C

Form: Free

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Example 529

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 213 - 215°C

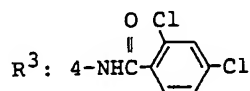
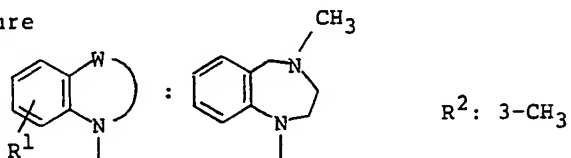
Form: Free

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Example 530

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

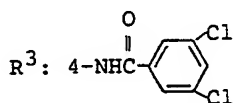
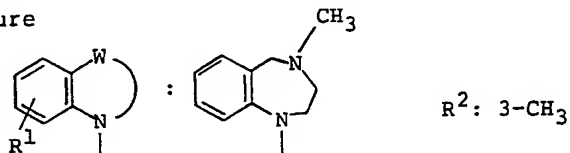
Melting Point: 167 - 167.5°C

Form: Free

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## Example 531

## Structure



Crystalline form: Colorless scales

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 217 - 221°C

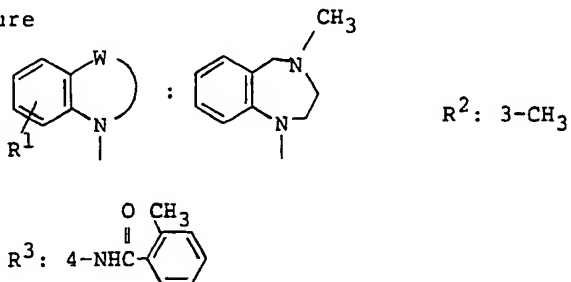
Form: Free

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Example 532

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

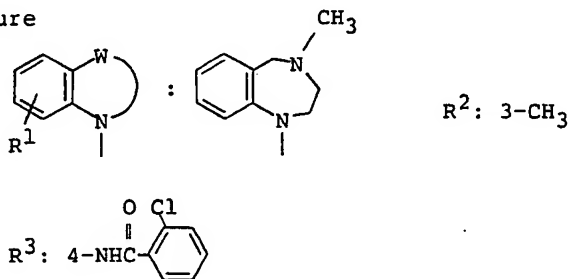
Melting Point: 182 - 184°C

Form: Free

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## Example 533

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 209 - 210°C

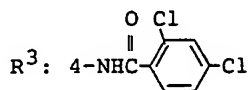
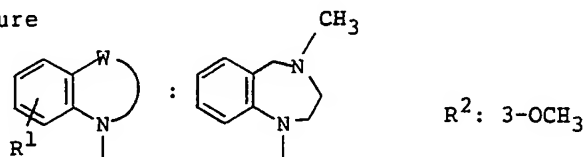
Form: Free

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Example 534

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

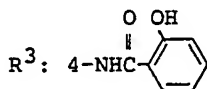
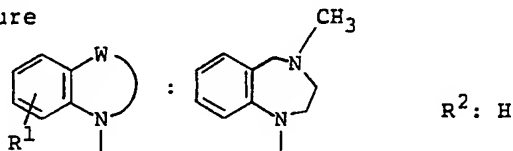
Melting Point: 148 - 149°C

Form: Free

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## Example 535

## Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 202 - 203°C

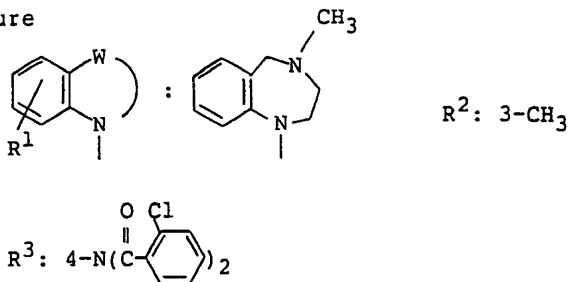
Form: Free

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Example 536

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

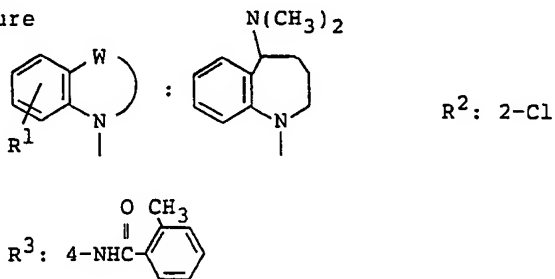
Melting Point: 218 - 219°C

Form: Free

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## Example 537

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/n-hexane

Melting Point: 159 - 160°C

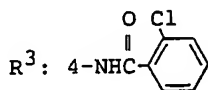
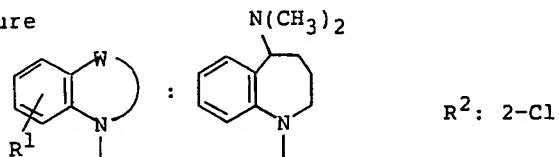
Form: Free

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Example 538

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/n-hexane

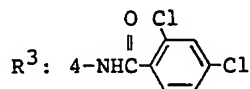
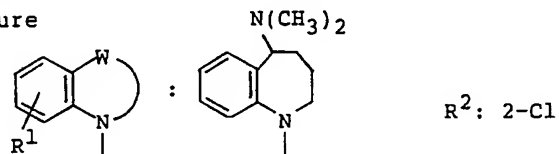
Melting Point: 201 - 202°C

Form: Free

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## Example 539

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/n-hexane

Melting Point: 205 - 207°C

Form: Free

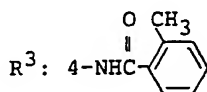
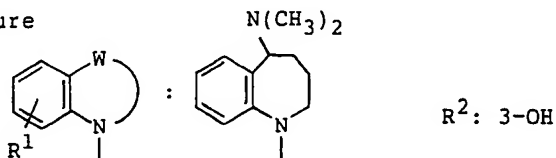
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Example 540

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

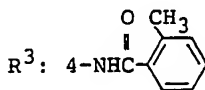
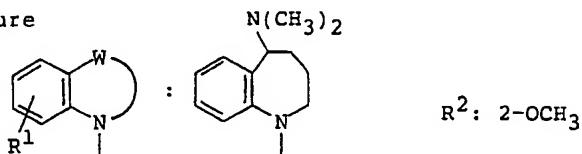
Melting Point: 201.5 - 202.5°C

Form: Free

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## Example 541

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

Melting Point: 226 - 228°C

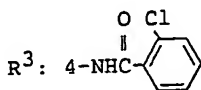
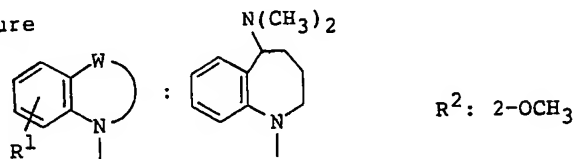
Form: Free

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Example 542

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

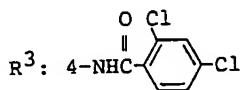
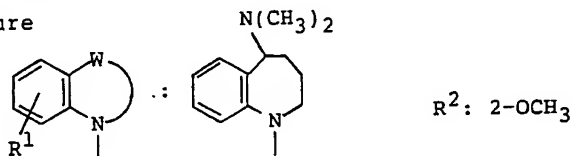
Melting Point: 218 - 221°C

Form: Free

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## Example 543

Structure



Crystalline form: White powder

Recrystallization solvent: Methanol/diethyl ether

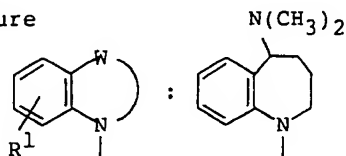
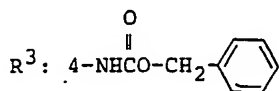
Melting Point: 156 - 157°C

Form: Free

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## Example 544

Structure

 $R^2: 2\text{-OCH}_3$ 

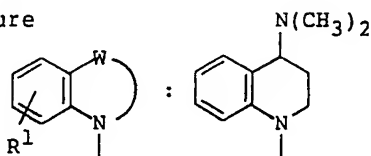
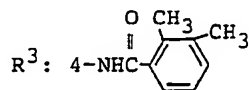
Crystalline form: White powder

NMR analysis: 80)

Form: Free

## Example 545

Structure

 $R^2: 3\text{-OCH}_3$ 

Crystalline form: Colorless amorphous .

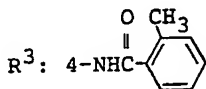
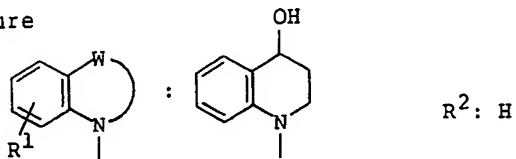
NMR analysis: 81)

Form: Free

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Example 546

Structure



Crystalline form: Colorless amorphous

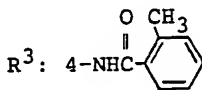
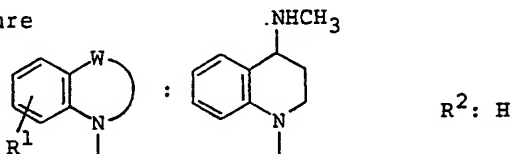
NMR analysis: 82)

Form: Free

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## Example 547

Structure



Crystalline form: Light yellow amorphous

NMR analysis: 83)

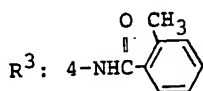
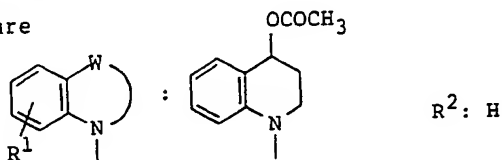
Form: Free

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Example 548

Structure



Crystalline form: Colorless amorphous

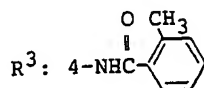
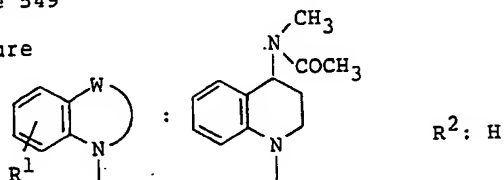
NMR analysis: 84).

Form: Free

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## Example 549

Structure



Crystalline form: Colorless amorphous

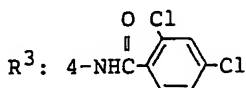
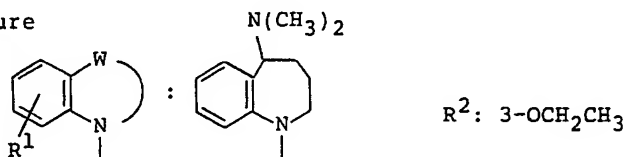
NMR analysis: 85)

Form: Free

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## Example 550

## Structure



Crystalline form: White powder

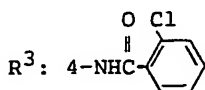
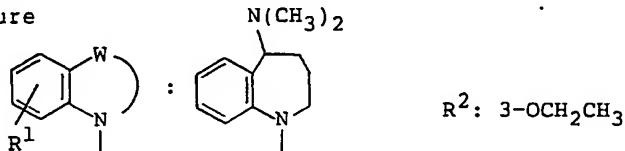
Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 135 - 136°C

Form: Free

## Example 551

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: n-Hexane/ethyl acetate

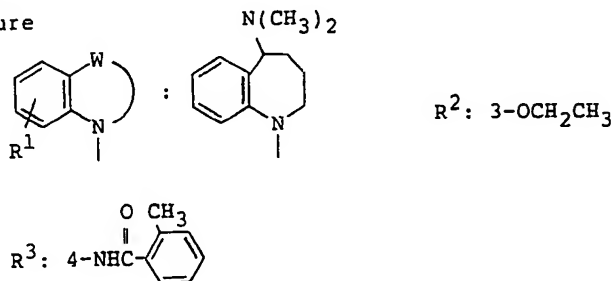
Melting Point: 122 - 123°C

Form: Free

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Example 552

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: n-Hexane/ethyl acetate

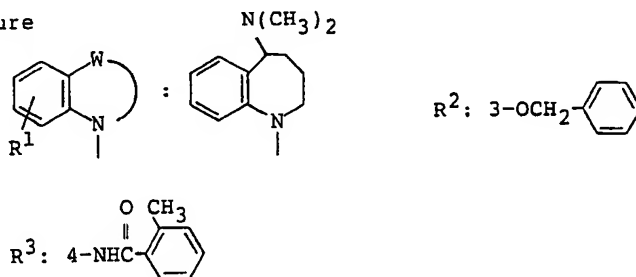
Melting Point: 118 - 119°C

Form: Free

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## Example 553

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 145 - 147°C

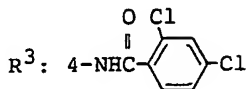
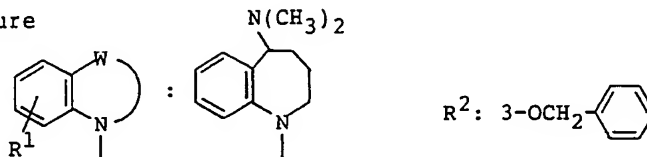
Form: Free

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Example 554

## Structure



Crystalline form: Light yellow needles

Recrystallization solvent: n-Hexane/ethyl acetate

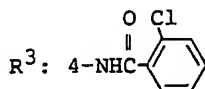
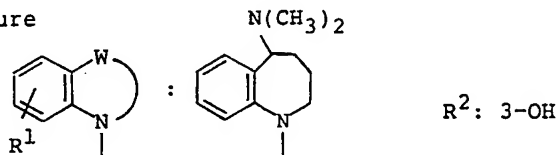
Melting Point: 169.5 - 170.5°C

Form: Free

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## Example 555

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: n-Hexane/ethyl acetate

Melting Point: 194 - 195°C

Form: Free

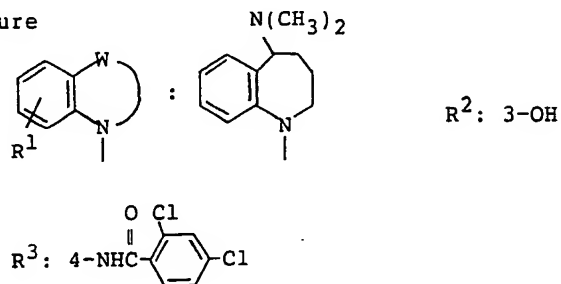
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Example 556

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: n-Hexane/ethyl acetate

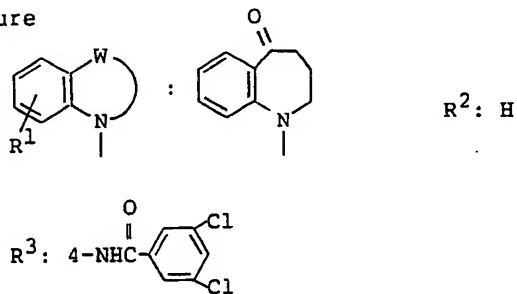
Melting Point: 202 - 204°C

Form: Free

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## Example 557

## Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

Melting Point: 242 - 243°C

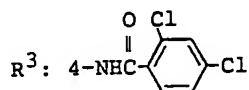
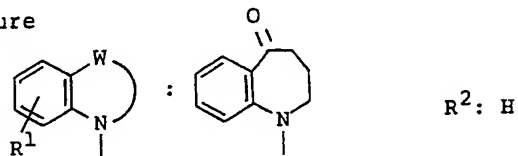
Form: Free

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Example 558

## Structure



Crystalline form: Light yellow powder

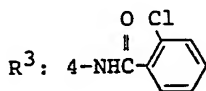
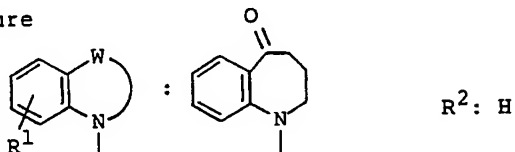
NMR analysis: 86)

Form: Free

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## Example 559

## Structure



Crystalline form: Light yellow powder

NMR analysis: 87)

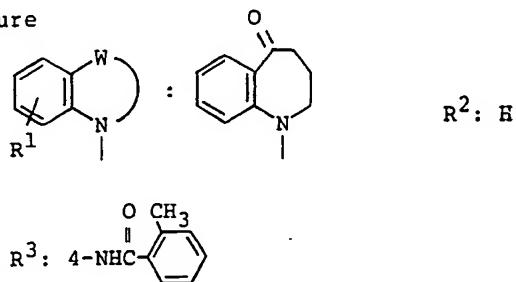
Form: Free

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Example 560

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

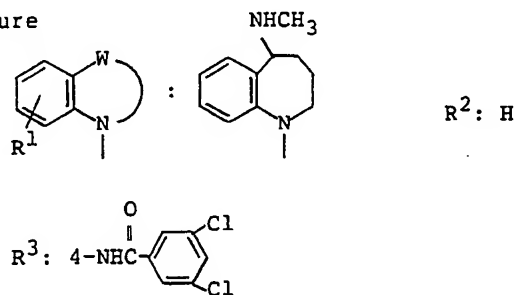
Melting Point: 237 - 238°C

Form: Free

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## Example 561

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Dioxane

Melting Point: 258 - 259°C

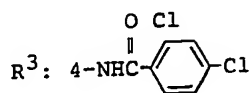
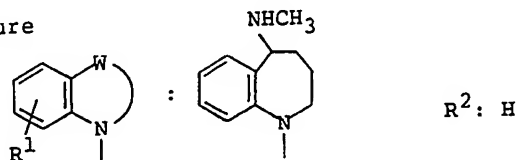
Form: Free

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Example 562

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

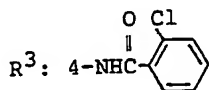
Melting Point: 182.5 - 183.5°C

Form: Free

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## Example 563

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

Melting Point: 209 - 211°C

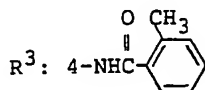
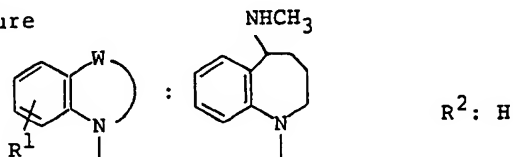
Form: Free

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Example 564

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Dioxane

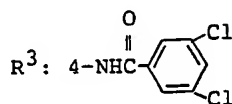
Melting Point: 210 - 211°C

Form: Free

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## Example 565

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 176 - 178°C

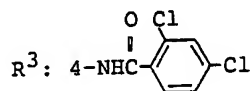
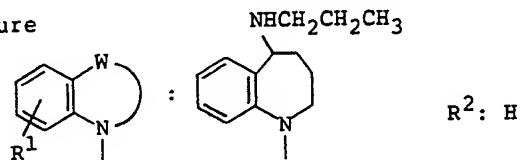
Form: Free

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Example 566

## Structure



Crystalline form: Light yellow amorphous

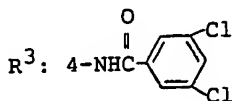
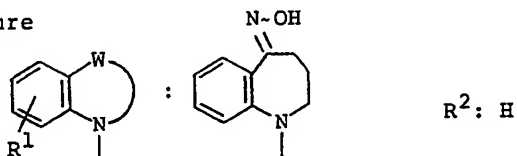
NMR analysis: 88)

Form: Free

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## Example 567

## Structure



Crystalline form: White powder

Recrystallization solvent: Dioxane/water

Melting Point: 272 - 273°C

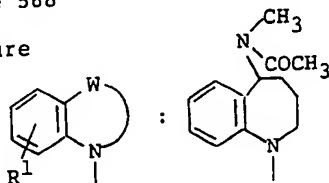
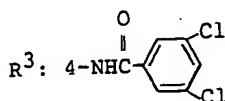
Form: Free

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Example 568

Structure

R<sup>2</sup>: H

Crystalline form: Colorless prisms

Recrystallization solvent: Dioxane

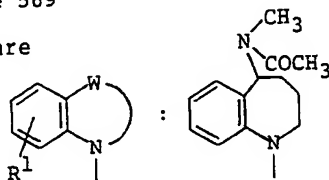
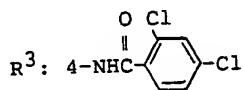
Melting Point: 253 - 254°C

Form: Free

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## Example 569

Structure

R<sup>2</sup>: H

Crystalline form: Colorless prisms

Recrystallization solvent: Ethanol

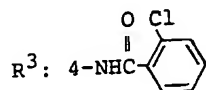
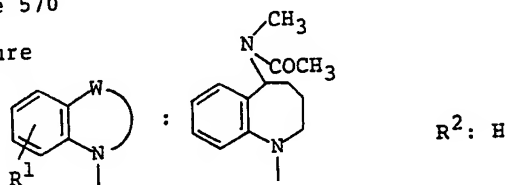
Melting Point: 248.5 - 249.5°C

Form: Free

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## Example 570

Structure



Crystalline form: Colorless needles

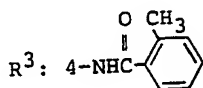
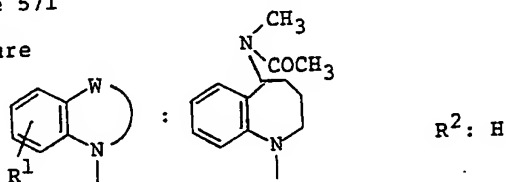
Recrystallization solvent: Ethanol

Melting Point: 266.5 - 267.5°C

Form: Free

## Example 571

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

Melting Point: 252 - 253°C

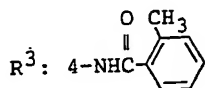
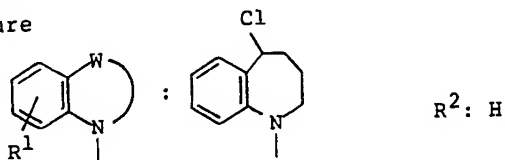
Form: Free



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Example 572

Structure



Crystalline form: Light yellow powder

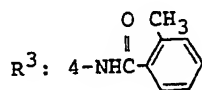
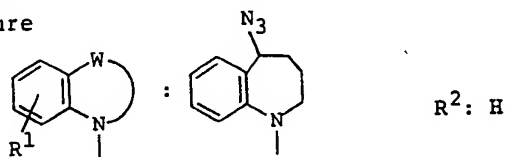
NMR analysis: 89)

Form: Free

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## Example 573

Structure



Crystalline form: Light brown powder

NMR analysis: 90)

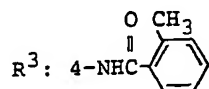
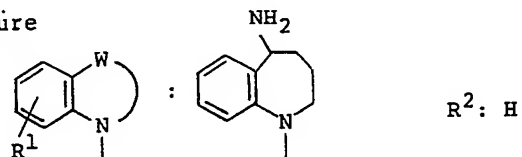
Form: Free

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Example 574

## Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether

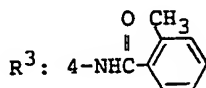
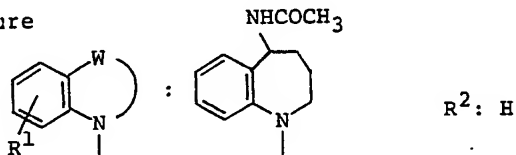
Melting Point: 198.5 - 199.5°C

Form: Free

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## Example 575

## Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

Melting Point: 297 - 299°C

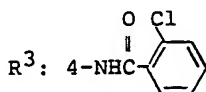
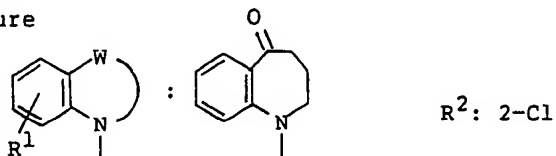
Form: Free

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Example 576

Structure



Crystalline form: Colorless amorphous

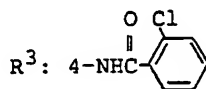
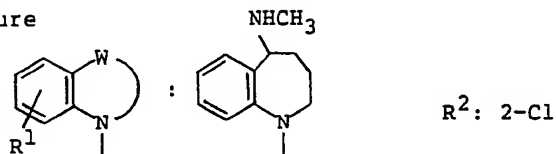
NMR analysis: 91)

Form: Free

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Example 577

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/petroleum ether

Melting Point: 202 - 203°C

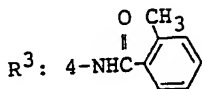
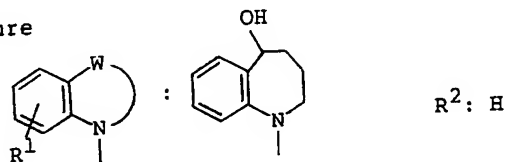
Form: Free

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Example 578

Structure



Crystalline form: Colorless amorphous

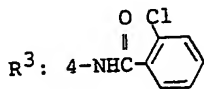
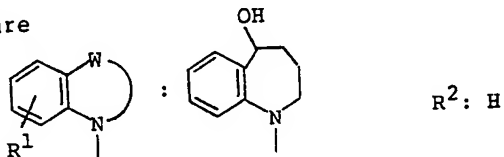
NMR analysis: 92)

Form: Free

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## Example 579

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 232 - 233°C

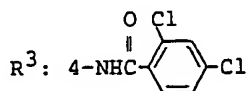
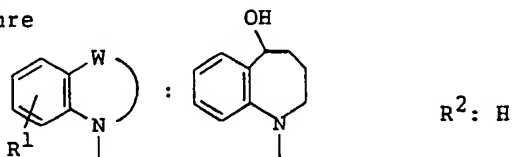
Form: Free

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Example 580

Structure



Crystalline form: Colorless amorphous

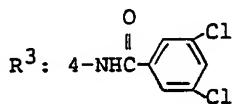
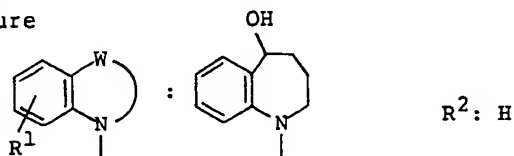
NMR analysis: 93)

Form: Free

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## Example 581

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 256.5 - 257°C

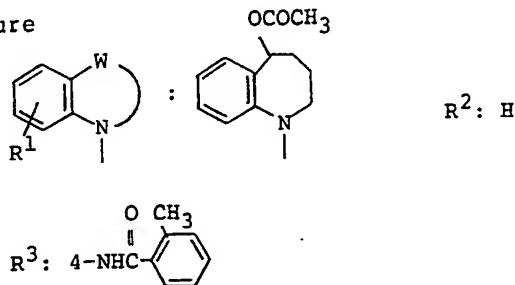
Form: Free

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Example 582

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

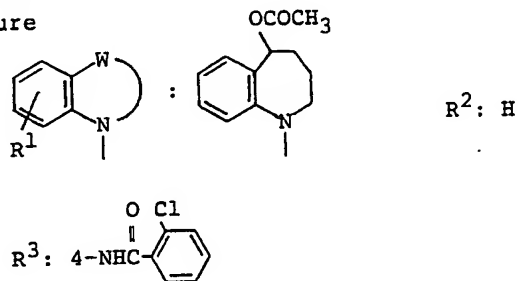
Melting Point: 193 - 194°C

Form: Free

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## Example 583

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 227 - 230°C

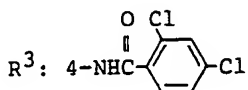
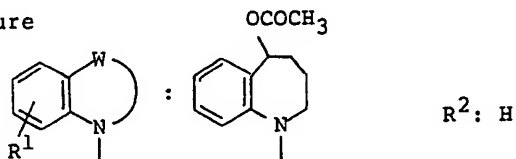
Form: Free

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Example 584

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

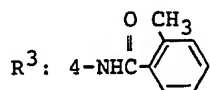
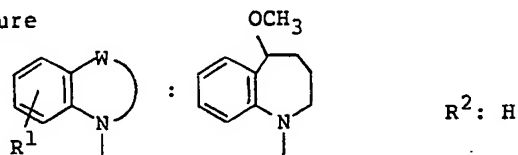
Melting Point: 199.5 - 202°C

Form: Free

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## Example 585

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 219 - 220°C

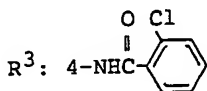
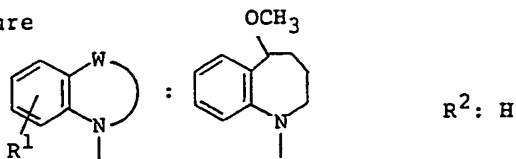
Form: Free

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Example 586

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

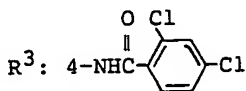
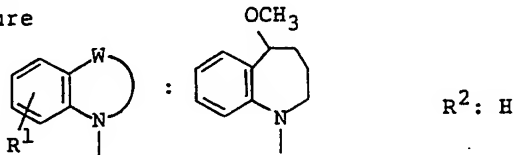
Melting Point: 190 - 191.5°C

Form: Free

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## Example 587

## Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 184 - 185°C

Form: Free

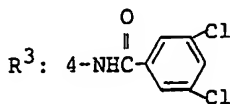
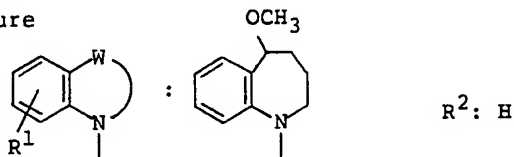
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Example 588

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

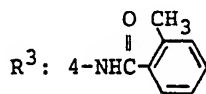
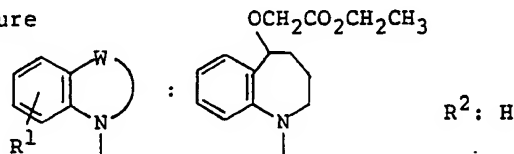
Melting Point: 223 - 224°C

Form: Free

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## Example 589

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 178 - 181°C

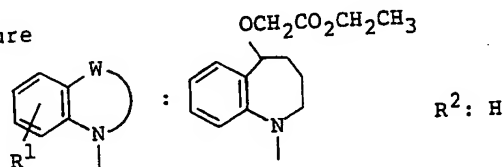
Form: Free

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Example 590

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethyl acetate/n-hexane

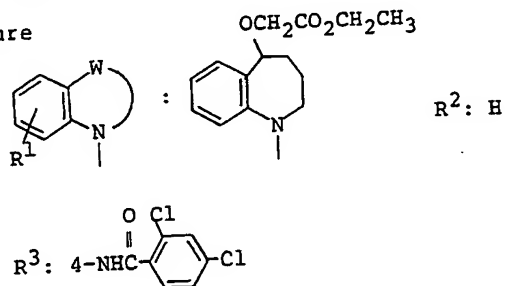
Melting Point: 168 - 168.5°C

Form: Free

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## Example 591

Structure



Crystalline form: Colorless amorphous

NMR analysis: 94)

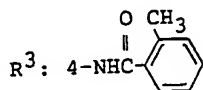
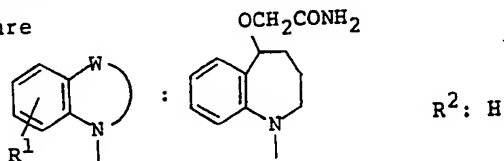
Form: Free

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Example 592

Structure



Crystalline form: Colorless amorphous

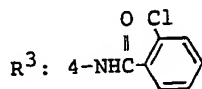
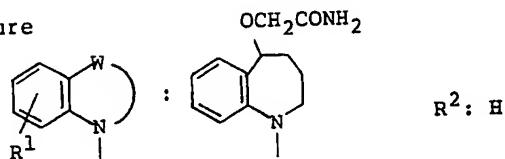
NMR analysis: 95)

Form: Free

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## Example 593

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 196 - 197°C

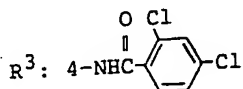
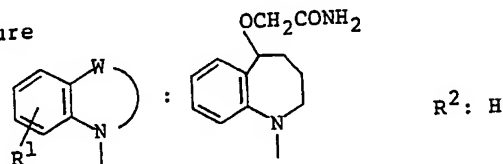
Form: Free

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Example 594

Structure



Crystalline form: Colorless amorphous

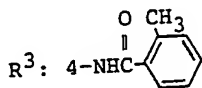
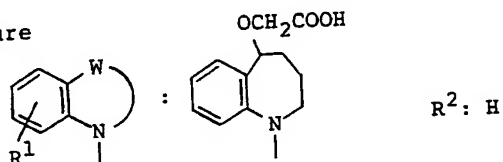
NMR analysis: 96)

Form: Free

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## Example 595

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol/water

Melting Point: 188 - 189°C

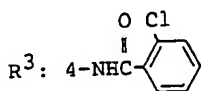
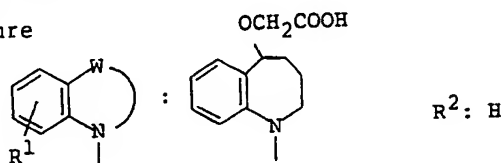
Form: Free

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Example 596

Structure



Crystalline form: Colorless amorphous

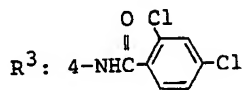
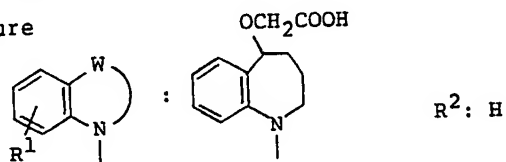
NMR analysis: 97)

Form: Free

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Example 597

Structure



Crystalline form: Colorless amorphous

NMR analysis: 98)

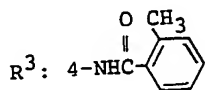
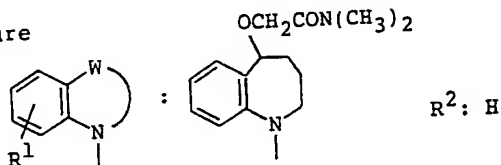
Form: Free

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Example 598

Structure



Crystalline form: Colorless prisms

Recrystallization solvent: Ethyl acetate/n-hexane

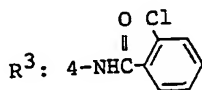
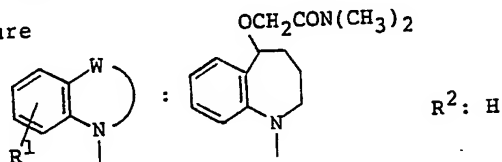
Melting Point: 203 - 204°C

Form: Free

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## Example 599

Structure



Crystalline form: White powder

Recrystallization solvent: Ethyl acetate/n-hexane

Melting Point: 196 - 197°C

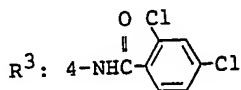
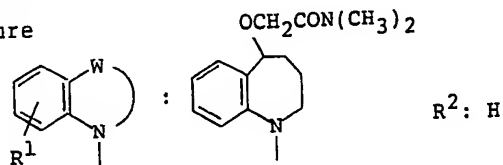
Form: Free

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Example 600

Structure



Crystalline form: Colorless amorphous

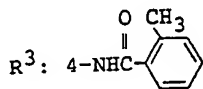
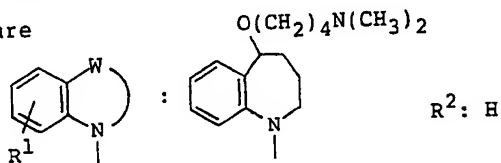
NMR analysis: 99)

Form: Free

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## Example 601

Structure



Crystalline form: Colorless amorphous

NMR analysis: 100)

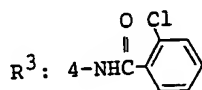
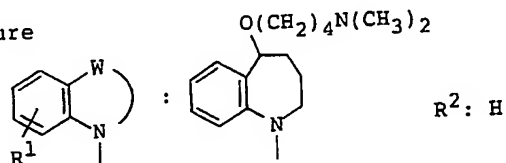
Form: Free

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Example 602

Structure



Crystalline form: Colorless amorphous

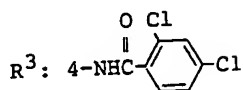
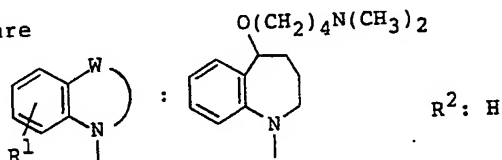
NMR analysis: 101)

Form: Free

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## Example 603

Structure



Crystalline form: Colorless amorphous .

NMR analysis: 102)

Form: Free

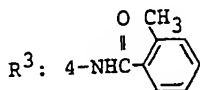
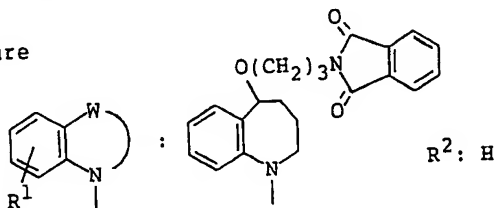
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Example 604

Structure



Crystalline form: Colorless amorphous

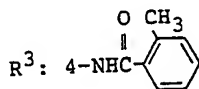
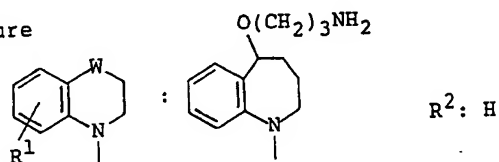
NMR analysis: 103)

Form: Free

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## Example 605

Structure



Crystalline form: Colorless amorphous

NMR analysis: 104)

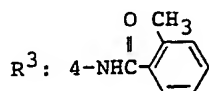
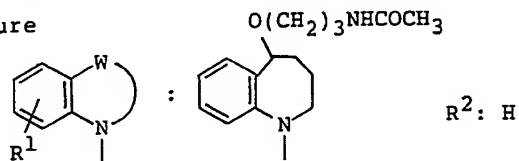
Form: Free

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Example 606

Structure



Crystalline form: Colorless amorphous

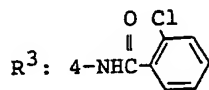
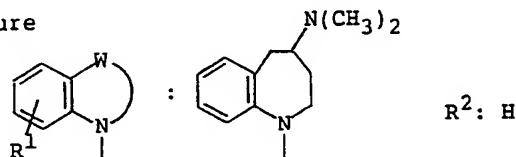
NMR analysis: 105)

Form: Free

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## Example 607

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol

Melting Point: 169 - 171°C

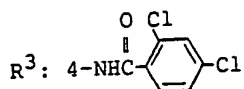
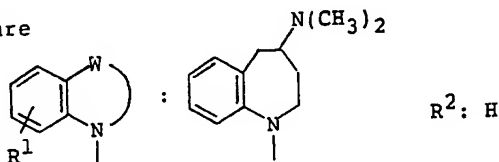
Form: Free

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Example 608

Structure



Crystalline form: Colorless needles

Recrystallization solvent: Ethanol/diethyl ether

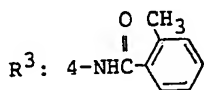
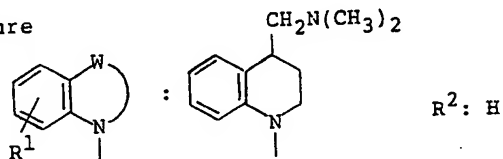
Melting Point: 178 - 181°C

Form: Free

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## Example 609

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 187 - 188°C

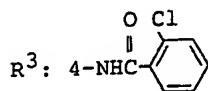
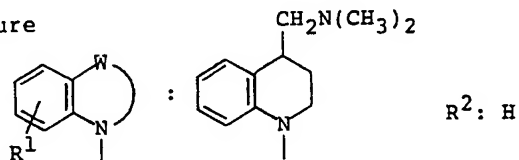
Form: Free

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Example 610

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

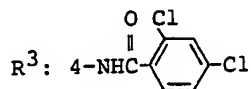
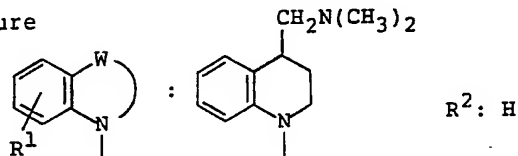
Melting Point: 181 - 183°C

Form: Free

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## Example 611

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

Melting Point: 124 - 127°C

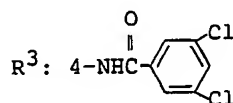
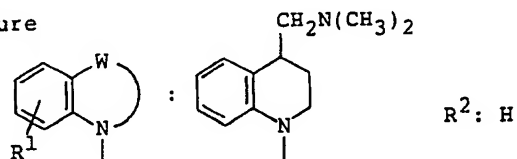
Form: Free

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Example 612

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

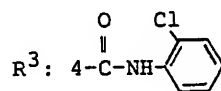
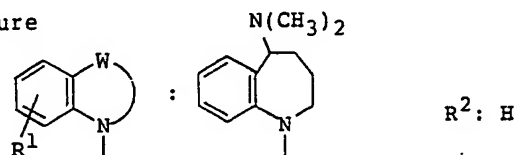
Melting Point: 179 - 181°C

Form: Free

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## Example 613

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

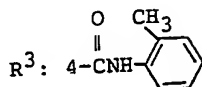
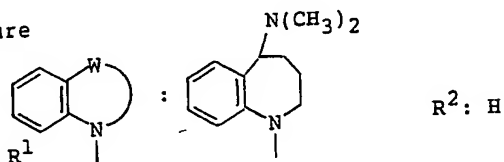
Melting Point: 148 - 150°C

Form: Free

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## Example 614

Structure



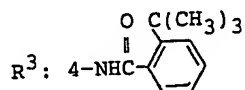
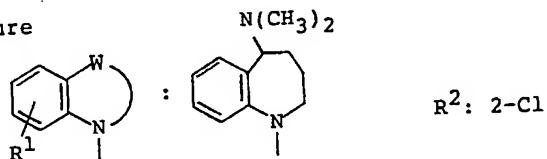
Crystalline form: Colorless amorphous

NMR analysis: 106)

Form: Free

## Example 615

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

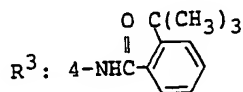
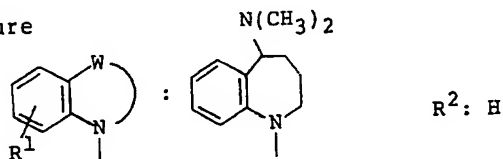
Melting Point: 219 - 220°C

Form: Free

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Example 616

Structure



Crystalline form: White powder

Recrystallization solvent: Ethanol

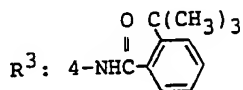
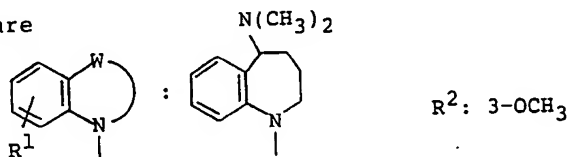
Melting Point: 226 - 228°C

Form: Free

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## Example 617

Structure



Crystalline form: Colorless amorphous

NMR analysis: 107)

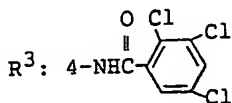
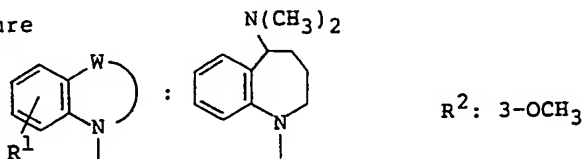
Form: Free

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Example 618

Structure



Crystalline form: Colorless amorphous

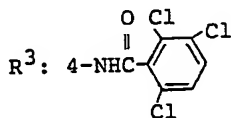
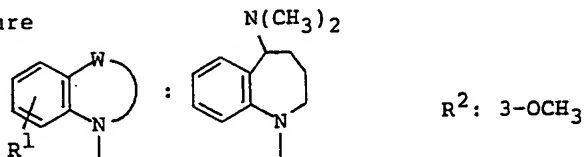
NMR analysis: 108)

Form: Free

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Example 619

Structure



Crystalline form: Colorless amorphous

NMR analysis: 109)

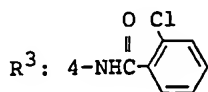
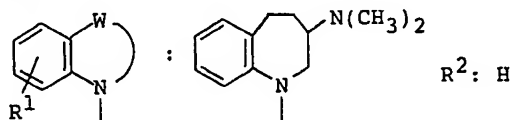
Form: Free



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Example 620

## Structure



Crystalline form: Colorless amorphous

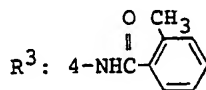
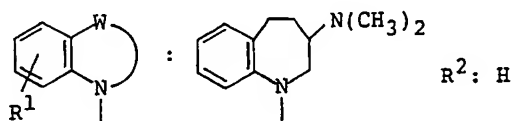
NMR analysis: 110)

Form: Free

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Example 621

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 111)

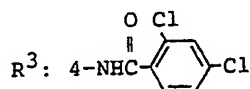
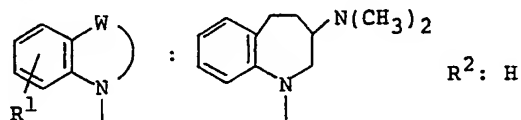
Form: Free

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Example 622

## Structure



Crystalline form: Colorless amorphous

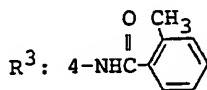
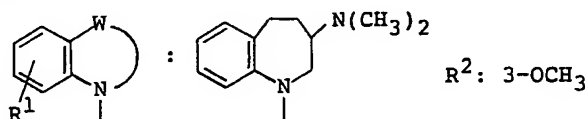
NMR analysis: 112)

Form: Free

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## Example 623

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 113)

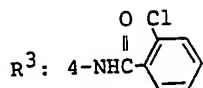
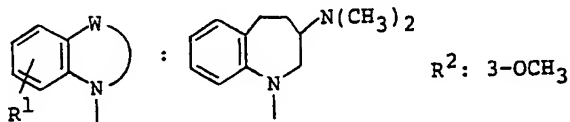
Form: Free

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Example 624

## Structure



Crystalline form: Colorless amorphous

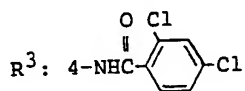
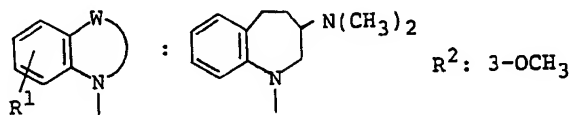
NMR analysis: 114)

Form: Free

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## Example 625

## Structure



Crystalline form: Colorless amorphous

NMR analysis: 115)

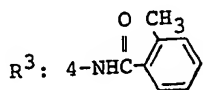
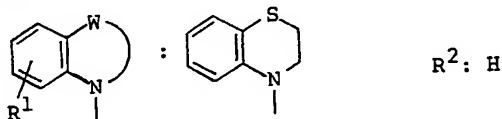
Form: Free

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Example 626

## Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

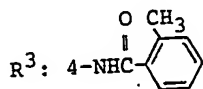
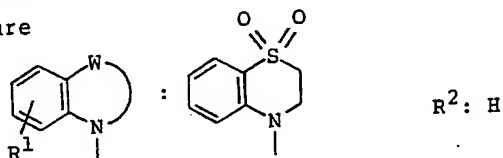
Melting Point: 183 - 184°C

Form: Free

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## Example 627

## Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

Melting Point: 219 - 220°C

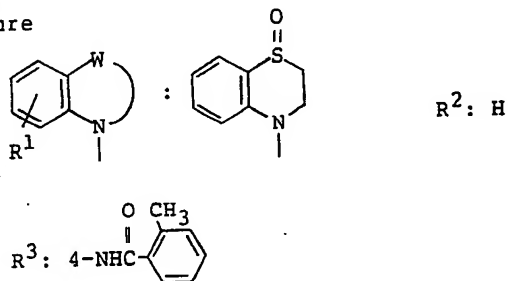
Form: Free

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Example 628

Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

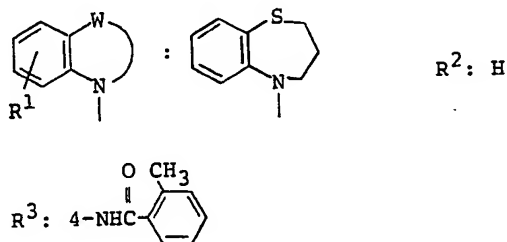
Melting Point: 240 - 241°C

Form: Free

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## Example 629

Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

Melting Point: 205 - 206°C

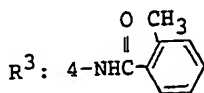
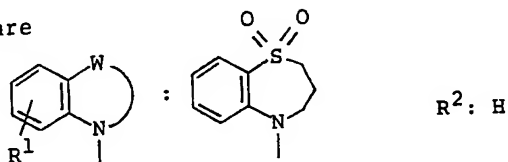
Form: Free

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Example 630

Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

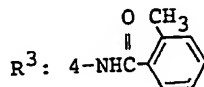
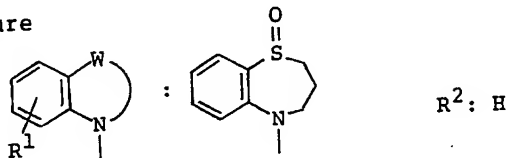
Melting Point: 238 - 239°C

Form: Free

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## Example 631

Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

Melting Point: 233 - 234°C

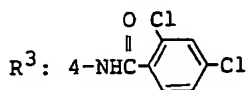
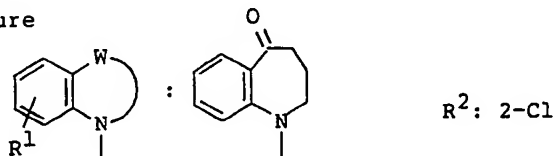
Form: Free

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Example 632

Structure



Crystalline form: Colorless amorphous

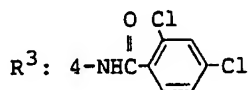
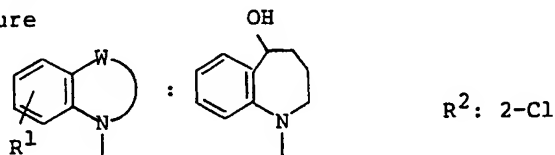
NMR analysis: 116)

Form: Free

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Example 633

Structure



Crystalline form: White powder

Recrystallization solvent: Diethyl ether/dichloromethane

Melting Point: 259.5 - 260.5°C

Form: Free

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- 80)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.24-5.26 (18H, m), 6.39-7.59 (13H, m)
- 81)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.70-2.10 (m, 2H), 2.15-2.60 (m, 12H), 3.56 (t, J=5.8 Hz, 1H), 3.65-3.95 (m, 4H), 4.05-4.25 (m, 1H), 6.64 (d, J=7.7 Hz, 1H), 6.85-7.50 (m, 9H), 8.11 (brs, 1H), 8.42 (d, J=8.8 Hz, 1H)
- 82)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.00-2.90 (m, 3H), 2.49 (s, 3H), 3.70-3.90 (m, 1H), 4.00-4.20 (m, 1H), 4.80-5.00 (m, 1H), 6.89 (d, J=6.3 Hz, 1H), 6.95-7.65 (m, 11H), 7.70 (brs, 1H)
- 83)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.95-2.90 (m, 2H), 2.48 (s, 3H), 2.55 (s, 3H), 3.77 (t, J=5.1 Hz, 1H), 3.92 (t, J=6.7 Hz, 2H), 6.72 (d, J=8.0 Hz, 1H), 6.90-7.15 (m, 2H), 7.15-7.70 (m, 9H), 7.81 (brs, 1H)
- 84)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 2.11 (s, 3H), 2.20-2.40 (m, 2H), 2.50 (s, 3H), 3.80-4.10 (m, 1H), 4.12-4.25 (m, 1H), 6.03 (t, J=4.3 Hz, 1H), 6.80-7.65 (m, 12H), 7.80 (brs, 1H)
- 85)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.80-2.40 (m, 5H), 2.45 (s, 3H), 2.81 (s, 3H), 3.55-3.82 (m, 1H), 4.15-4.40 (m, 1H), 5.90-6.10 (m, 1H), 6.80-7.80 (m, 12H), 8.67 (brs, 1H)
- 86)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.95-2.35 (2H, m), 2.75-3.0 (2H, m), 3.0-5.4 (2H, m), 6.55-7.95 (11H, m), 8.09 (1H, s)



- 87)  $^1\text{H-NMR}(\text{DMSO}-d_6) \delta$  ; 1.85-2.2 (2H, m), 2.7-2.95 (2H, m), 3.5-5.0 (2H, m), 6.8-7.8 (12H, m), 10.60 (1H, s)
- 88)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 0.8-1.1 (3H, m), 1.2-2.35 (6H, m), 2.35-5.25 (6H, m), 6.63 (1H, d,  $J=7.7$  Hz), 6.8-7.6 (9H, m), 7.67 (1H, d,  $J=8.2$  Hz), 7.9-8.15 (1H, m)
- 89)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 1.7-2.9 (7H, m), 4.5-6.5 (3H, m), 6.55-6.75 (1H, m), 6.85-7.6 (12H, m)
- 90)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 1.65-3.1 (7H, m), 4.7-6.6 (3H, m), 6.6-6.8 (1H, m), 6.85-7.65 (12H, m)
- 91)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 1.8-2.4 (2H, m), 2.86 (2H, t,  $J=6$  Hz), 3.1-5.15 (2H, m), 6.85-7.5 (8H, m), 7.5-7.85 (3H, m), 8.19 (1H, s)
- 92)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 1.46-2.28 (4H, m), 2.37 (3H, s), 2.58-2.90 (1H, m), 4.57-5.10 (2H, m), 6.59 (1H, d,  $J=7.6$  Hz), 6.91-7.52 (11H, m), 7.62 (1H, d,  $J=7.6$  Hz), 8.10-8.40 (1H, m)
- 93)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 1.45-1.91 (2H, m), 1.91-2.65 (2H, m), 2.65-2.90 (1H, m), 4.63-5.22 (2H, m), 6.63 (1H, d,  $J=7.4$  Hz), 7.34-8.03 (11H, m), 10.16-10.44 (1H, m)
- 94)  $^1\text{H-NMR}(\text{CDCl}_3) \delta$  ; 1.08-1.47 (3H, m), 1.50-1.97 (2H, m), 1.97-2.48 (2H, m), 2.65-3.02 (1H, m), 4.00-4.43 (4H, m), 4.52-5.15 (2H, m), 6.50-6.79 (1H, m), 6.90-7.70 (10H, m), 8.26-8.60 (1H, m)

- 95)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.56-2.67 (4H, m), 2.46 (3H, s),  
2.67-3.03 (1H, m), 3.82-4.32 (2H, m), 4.45-5.15  
(2H, m), 5.43-5.83 (1H, m), 6.20-6.45 (1H, m),  
6.50-6.86 (2H, m), 6.86-7.70 (10H, m), 7.76-8.10  
(1H, m)
- 96)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.52-1.90 (2H, m), 1.90-2.54 (2H,  
m), 2.67-3.05 (1H, m), 3.74-4.32 (2H, m), 4.38-5.17  
(2H, m), 5.52-5.98 (1H, brs), 6.20-6.48 (1H, brs),  
6.55-6.84 (1H, m), 6.89-7.55 (9H, m), 7.55-7.77  
(1H, m), 8.15-8.86 (1H, brs)
- 97)  $^1\text{H-NMR}(\text{DMSO}-d_6)$   $\delta$  ; 1.26-2.49 (4H, m), 2.57-2.93  
(1H, m), 4.07-4.43 (2H, m), 4.44-4.98 (2H, m),  
6.62-6.87 (1H, m), 6.92-7.80 (11H, m), 10.57 (1H,  
s), 12.74 (1H, s)
- 98)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.52-1.89 (2H, m), 1.89-2.56 (2H,  
m), 2.65-3.02 (1H, m), 3.90-4.40 (2H, m), 4.40-5.07  
(2H, m), 6.58-6.78 (1H, m), 6.90-7.70 (10H, m),  
8.57-8.81 (1H, brs)
- 99)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.49-1.89 (2H, m), 1.89-2.60 (2H,  
m), 2.63-3.23 (7H, m), 4.04-4.49 (2H, m), 4.52-5.21  
(2H, m), 6.52-6.80 (1H, m), 6.89-7.84 (10H, m),  
8.08-8.52 (1H, m)
- 100)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.41-1.86 (6H, m), 1.86-2.53 (4H,  
m), 2.25 (3H, s), 2.29 (3H, s), 2.43 (3H, s), 2.60-  
2.97 (1H, m), 3.36-3.77 (2H, m), 4.40-5.10 (2H, m),  
6.54-6.72 (1H, m), 6.88-7.67 (11H, m), 8.27-8.58

- (1H, m)
- 101)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.44-1.85 (6H, m), 1.85-2.61 (4H, m), 2.32 (3H, s), 2.35 (3H, s), 2.61-3.00 (1H, m), 3.33-3.76 (2H, m), 4.40-5.20 (2H, m), 6.57-6.75 (1H, m), 6.90 - 7.70 (11H, m), 8.50-8.93 (1H, m)
- 102)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.49-2.04 (6H, m), 2.10-3.02 (5H, m), 2.47 (6H, s), 3.40-3.88 (2H, m), 4.30-5.17 (2H, m), 6.59-6.78 (1H, m), 6.93-7.76 (10H, m), 8.75-9.40 (1H, m)
- 103)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.47-2.47 (6H, m), 2.44 (3H, s), 2.62-3.03 (1H, m), 3.47-4.03 (4H, m), 4.48-5.17 (2H, m), 6.51-6.74 (1H, m), 6.87-7.62 (11H, m), 7.62-7.77 (2H, m), 7.77-8.03 (3H, m)
- 104)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.42-2.32 (6H, m), 2.44 (3H, s), 2.57-2.97 (1H, m), 3.12-3.83 (4H, m), 4.39-5.13 (2H, m), 6.50-6.71 (1H, m), 6.90-7.73 (12H, m)
- 105)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.50-2.63 (9H, m), 2.47 (3H, s), 2.66-3.07 (1H, m), 3.10-3.88 (4H, m), 4.40-5.17 (2H, m), 5.87-6.23 (1H, brs), 6.60-6.79 (1H, m), 6.94-7.60 (11H, m), 7.67 (1H, s)
- 106)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.20-2.53 (13H, m), 2.63-2.82, 3.00-3.13, 3.50-3.67, 4.05-4.23 (total 3H, m), 6.55 - 8.00 (13H, m)
- 107)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.41 (9H, s), 1.20-2.55 (10H, m), 3.42-4.20 (5.8H, m), 5.00-5.20 (0.2H, m), 6.60-7.67 (10H, m), 7.99 (1H, brs), 8.26 (1H, d,  $J=8.4$  Hz)

- 108)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.2-3.0 (10H, m), 3.0-5.2 (6H, m), 6.5-7.7 (8H, m), 8.22 (1H, d,  $J=8.4$  Hz), 8.36 (1H, s)
- 109)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.2-3.0 (10H, m), 3.0-5.2 (6H, m), 6.3-7.7 (10H, m)
- 110)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.5-1.7 (1H, m), 2.2-2.7 (2H, m), 2.40 (6H, s), 2.7-3.0 (3H, m), 5.1-5.3 (1H, m), 6.67 (1H, d,  $J=7.7$  Hz), 6.9-7.5 (10H, m), 7.69 (1H, d,  $J=6$  Hz), 8.06 (1H, s)
- 111)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.4-1.7 (1H, m), 2.1-2.7 (2H, m), 2.40 (6H, s), 2.44 (3H, s), 2.7-3.0 (3H, m), 5.1-5.3 (1H, m), 6.68 (1H, d,  $J=7.8$  Hz), 6.9-7.5 (11H, m), 7.66 (1H, s)
- 112)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.5-1.8 (1H, m), 2.1-2.7 (2H, m), 2.38 (6H, s), 2.7-3.0 (3H, m), 5.1-5.3 (1H, m), 6.66 (1H, d,  $J=7.7$  Hz), 6.9-7.0 (9H, m), 7.57 (1H, d,  $J=8.3$  Hz), 8.42 (1H, s)
- 113)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.5-1.8 (1H, m), 2.1-2.7 (2H, m), 2.41 (6H, s), 2.48 (3H, s), 2.7-3.0 (3H, m), 3.68 (3H, s), 5.2-5.4 (1H, m), 6.6-6.8 (2H, m), 6.9-7.5 (8H, m), 8.09 (1H, s), 8.26 (1H, d,  $J=8.1$  Hz)
- 114)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.5-1.7 (1H, m), 2.1-2.3 (1H, m), 2.41 (6H, s), 2.4-2.6 (1H, m), 2.8-3.0 (3H, m), 3.71 (3H, s), 5.2-5.4 (1H, m), 6.6-6.8 (2H, m), 6.9-7.5 (7H, m), 7.7-7.8 (1H, m), 8.27 (1H, d,  $J=8.4$  Hz), 8.57 (1H, s)

- 115)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.5-1.7 (1H, m), 2.1-2.7 (2H, m), 2.41 (6H, s), 2.7-3.0 (3H, m), 3.71 (3H, s), 5.2-5.4 (1H, m), 6.6-7.6 (8H, m), 7.70 (1H, d,  $J=8.3$  Hz), 8.24 (1H, d,  $J=8.5$  Hz), 8.59 (1H, s)
- 116)  $^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.8-2.3 (3H, m), 2.7-2.9 (2H, m), 3.5-3.7 (1H, m), 6.8-8.0 (10H, m), 8.7-9.1 (1H, br)

Example 634

To a mixture of 5-oxo-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (4 g) and pyridine (50 ml) is added hydroxylamine hydrochloride (1.84 g) and the mixture is refluxed for 2.5 hours. The reaction solution is concentrated and water is added to the resulting residue. The precipitated crystal is collected by filtration, and recrystallized from dioxane/water to give 5-hydroxyimino-1-[4-(3,5-dichlorobenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (2 g) as white powder, m.p. 272 - 273°C.

Example 635

5-Chloro-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.8 g) is dissolved in dimethylformamide and thereto is added sodium azide (0.18 g) at room temperature. The mixture is stirred at room temperature overnight, and further reacted with heating at 50°C for 5 hours. Water is added to the reaction mixture and the precipitated crystal is collected by filtration to give 5-azido-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-

tetrahydro-1H-benzazepine (0.68 g) as light brown powder.

$^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.65-3.1 (8H, m), 4.7-6.6 (3H, m), 6.6-6.8 (1H, m), 6.85-7.65 (12H, m)

Example 636

5-Azido-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.63 g) is dissolved in ethanol and thereto is added 10 % Pd-C (0.1 g). The mixture is subjected to catalytic hydrogenation at room temperature under 1 atm. of hydrogen. Pd-C is removed by filtration and the filtrate is evaporated. The resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 50 : 1), and recrystallized from diethyl ether to give 5-amino-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.34 g) as white powder, m.p. 198.5 - 199.5°C.

Example 637

To 5-hydroxy-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.58 g) are added acetic anhydride (8.0 ml) and pyridine (2.0 ml). The mixture is stirred at room temperature for 1 hour. Water is added to the reaction mixture and the precipitated crystal is collected by filtration, and recrystallized from ethyl acetate/n-hexane to give 5-acetyloxy-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.56 g) as white powder, m.p. 193 - 194°C.

Example 638

5-Ethoxycarbonylmethoxy-1-[4-(2-methylbenzoyl-amino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (1.00 g) is dissolved in methanol (35 ml) and thereto are added aqueous ammonia (20 ml) and ammonium chloride (0.50 g). The mixture is heated at 100°C for 3.5 hours in a sealed tube. After cooling, the reaction solution is concentrated under reduced pressure and acidified with hydrochloric acid, and extracted with dichloromethane. The extract is dried over magnesium sulfate and the solvent is distilled off. The resulting residue is purified by silica gel column chromatography (eluent; dichloromethane : methanol = 15 : 1) to give 5-carbamoylmethoxy-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.68 g) as colorless amorphous.

$^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.56-2.67 (4H, m), 2.46 (3H, s), 2.67-3.03 (1H, m), 3.82-4.32 (2H, m), 4.45-5.15 (2H, m), 5.43-5.83 (1H, m), 6.20-6.45 (1H, m), 6.50-6.86 (2H, m), 6.86-7.70 (10H, m), 7.76-8.10 (1H, m)

Using the suitable starting materials, the compounds of the above Examples 593 and 594 are obtained in the same manner as in Example 638.

#### Example 639

5-Ethoxycarbonylmethoxy-1-[4-(2,4-dichlorobenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.94 g) is dissolved in ethanol (100 ml) and thereto is added 5N aqueous sodium hydroxide solution (0.50 ml). The mixture is

stirred at room temperature for 2 hours. The reaction solution is concentrated under reduced pressure and to the resulting residue is added diluted hydrochloric acid and then extracted with dichloromethane. The extract is dried over magnesium sulfate and the solvent is distilled off. The resulting residue is washed with n-hexane and collected by filtration to give 5-carboxymethoxy-1-[4-(2,4-dichlorobenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.79 g) as colorless amorphous.

$^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.52-1.89 (2H, m), 1.89-2.56 (2H, m), 2.65-3.02 (1H, m), 3.90-4.40 (2H, m), 4.40-5.07 (2H, m), 6.58-6.78 (1H, m), 6.90-7.70 (10H, m), 8.57-8.81 (1H, brs)

Using the suitable starting materials, the compounds of the above Examples 595 and 596 are obtained in the same manner as in Example 639.

#### Example 640

5-Carboxymethoxy-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.55 g) is dissolved in dimethylformamide (20 ml) and thereto are added dimethylamine hydrochloride (0.20 g) and diethyl chlorophosphate (0.33 g). To the mixture is added triethylamine (1.0 ml) under ice-cooling, and the mixture is stirred under ice-cooling for 30 minutes, and at room temperature for more 2 hours. Water is added to the reaction solution and the precipitated crystal is collected by filtration and crystallized from ethyl acetate/n-hexane to give 5-



dimethylaminocarbonylmethoxy-1-[4-(2-methylbenzoylamino)-benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.50 g) as colorless prisms, m.p. 203 - 204°C.

Using the suitable starting materials, the compounds of the above Examples 599 and 600 are obtained in the same manner as in Example 640.

Example 641

5-[3-(Phthalimid-1-yl)propoxy]-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (1.26 g) is dissolved in ethanol (100 ml) and thereto is added hydrazine hydrate (1.0 ml). The mixture is refluxed with stirring for 1 hour. The reaction solution is evaporated under reduced pressure and to the resulting residue is added dichloromethane. The insoluble materials are removed by filtration. The filtrate is purified by silica gel column chromatography (eluent; dichloromethane : methanol : aqueous ammonia = 70 : 10 : 1) to give 5-(3-aminopropoxy)-1-[4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.70 g) as colorless amorphous.

$^1\text{H-NMR}(\text{CDCl}_3)$   $\delta$  ; 1.42-2.32 (6H, m), 2.44 (3H, s), 2.57-2.97 (1H, m), 3.12-3.83 (4H, m), 4.39-5.13 (2H, m), 6.50-6.71 (1H, m), 6.90-7.73 (12H, m)

Example 642

A solution of 5-dimethylamino-1-[3-methoxy-4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-

benzazepine (0.50 g) in dichloromethane (30 ml) is added dropwise to a solution of 1M boron tribromide in dichloromethane (5.46 ml) at -45°C. After completion of the dropping, the mixture is stirred for 1 day while the temperature of the reaction mixture is gradually raised to room temperature. To the reaction solution is added water and the mixture is neutralized with sodium hydrogen carbonate, and extracted with dichloromethane. The extract is washed with saturated saline solution and dried over magnesium sulfate. The solvent is distilled off and the resulting residue is purified by silica gel column chromatography (eluent; chloroform : methanol = 500 : 1), and recrystallized from methanol/diethyl ether to give 5-dimethylamino-1-[3-hydroxy-4-(2-methylbenzoylamino)benzoyl]-2,3,4,5-tetrahydro-1H-benzazepine (0.33 g) as white powder, m.p. 201.5 - 202.5°C.

Using the suitable starting materials, the compounds of the above Examples 10, 32, 343, 356, 535, 555 and 556 are obtained in the same manner as in Example 642.

#### Example 643

To a solution of 4-[4-(2-methylbenzoylamino)-benzoyl]-3,4-dihydro-2H-1,4-benzazepine (0.5 g) in dichloromethane (10 ml) is added m-chloroperbenzoic acid (0.58 g) under ice-cooling, and the mixture is stirred at room temperature for 6 hours. The above reaction solution is poured into an aqueous solution of sodium carbonate (0.6 g) in water (10 ml) and the mixture is extracted with dichloro-